VOLUME 43 NUMBER 4

ARCHIVES OF

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CONTENTS OF PREVIOUS NUMBER

MARCH 1950. NUMBER 3

Late Fistulization of Operative Wounds: Diagnosis and Treatment. John H. Dunnington, M.D., New York, and Ellen F. Regan, M.D., Framingham, Mass.

Treatment of Retinitis Pigmentosa with Cod Liver Oil Injections and Placental Implantation. Samuel L. Salzmann, M.D., and Charles Haig, Ph.D., New York.

Use of Paraaminosalicylic Acid Alone or in Association with Streptomycin in Ocular Tuberculosis: Experimental and Clinical Investigations. G. B. Bietti, M.D., Pavia, Italy.

Dihydrine Sulfate: Comparative Clinical Study of Cycloplegic Effects. Bernard C. Cotton, M.D., Philadelphia.

Acute Retrobulbar Neuritis: Report of Two Cases. Robert T. Wong, M.D., Honolulu, T. H.

Hyperphoria: A Statistical Study. Richard G. Scobee, M.D., and Elizabeth A. Bennet, B.A., St. Louis.

Age Norms of Refraction and Vision. F. J. Sloaper, M.D., Houston, Texas.

The Eye in Tetanus: Report of a Case and Review of the Literature. Goodwin M. Breinin, M.D., New York.

Aneurysm of the Internal Carotid Artery Simulating Tumor: Report of a Case. Jesse M. Levitt, M.D., Brooklyn.

Corneal Fistula Following Transplantation: Report of Two Cases; Methods of Treatment. Charles I. Thomas, M.D., Cleveland.

Epithelial Invasion of Anterior Chamber Following Cataract Extraction: Effect of Radiation Therapy. Morris H. Pincus, M.D., Brooklyn.

Treatment of Giant Follicular Lymphoma with Nitrogen Mustard (Methyl-bis-[2-Chloroethyl]-Amine): Report of a Case. Benjamin M. Chambers, M.D., Philadelphia.

Absorption of Protein Through the Conjunctival Mucous Membrane. Robert A. Chait, M.D., Brooklyn.

Objective Testing of Vision with Use of the Galvanic Skin Response. Henry N. Wagner Jr., Baltimore.

Early Diagnosis of Syphilitic Primary Optic Nerve Atrophy. Joseph V. Klauder, M.D., Philadelphia, and George P. Mayer, M.D., Camden, N. J.

Clinical Notes:

Transformer for the A O "Glaucoma." John L. Goff, M.D., Boston.

Muscle Hook. David E. Roff, M.D., Cleveland.

A Fixation Aid for Slit Lamp Biomicroscopy. David D. Donaldson, M.D., and David G. Cogan, M.D., Boston.

News and Notes.

Obituaries:

Flinio E. Montalvio, M.D.

Abstracts from Current Literature.

Society Transactions:

New York Academy of Medicine, Section of Ophthalmology.

New England Ophthalmological Society.

Société Française d'Ophtalmologie.

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A SCIENTIFIC CORNER

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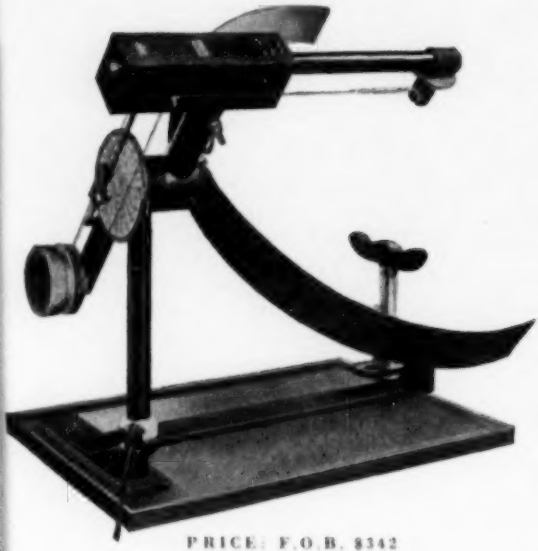

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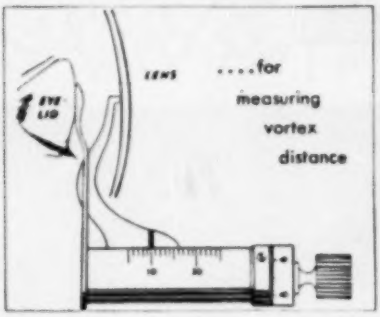

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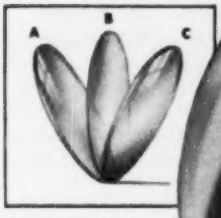
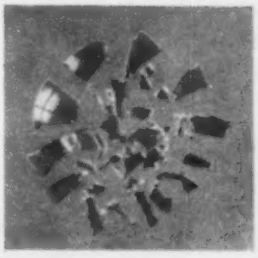


A. *Crown Glass*
B. *Lamina*
C. *Crown Glass*

A. *Ordinary glass lens after shatter test, showing how lens breaks into fragments.*

B. *Subjected to shatter test, I-Safe Lens does not fly apart, is therefore safe.*



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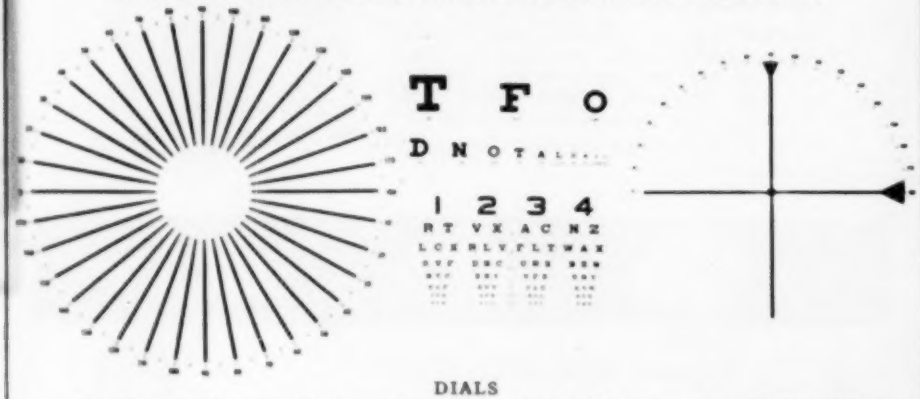

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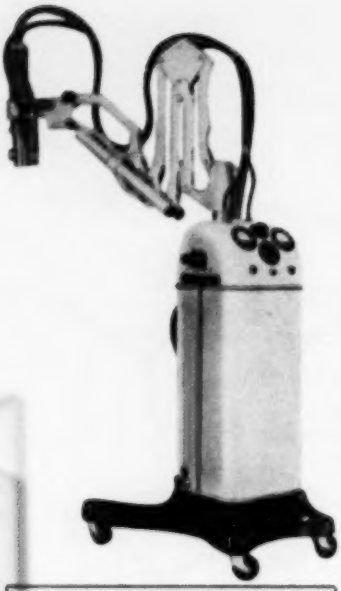

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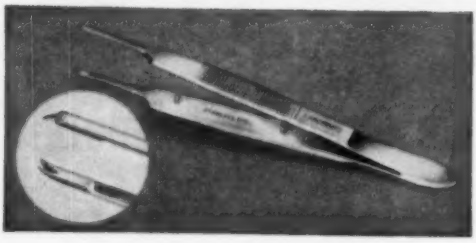

This forceps is a modification of that suggested by Dr. St. Martin. It is extremely useful in keratoplasty and keratectomy when doing marginal sutures and is also a valuable aid in scleral suturing. Sturdily constructed of stainless steel.

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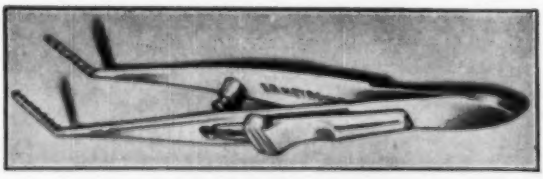

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ARCHIVES OF OPHTHALMOLOGY

VOLUME 43 APRIL 1950 NUMBER 4

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GROWTH OF THE COMPONENTS OF THE HUMAN EYEBALL

I. DIAGRAMS, CALCULATIONS, COMPUTATION AND REFERENCE TABLES

HARRY A. WILMER, M.D., Ph.D.*
PALO ALTO, CALIF.
AND
RICHARD E. SCAMMON, Ph.D.‡
BRANSON, MO.

QUANTITATIVE data on the dimensions of the eyeball as a whole and on many of its component structures have been reported in the medical and biologic literature over a long period. A number of observations have been visualized in the form of two dimensional reconstructions, commonly of median sagittal sections of the eyeball and its parts. Many of these figures are frankly schematic or semischematic. Nonetheless, they fulfil the purpose for which they were constructed, for they give clear, useful and approximately correct representations of the mean size and the spatial relations of the optic apparatus. A smaller number of two dimensional reconstructions have been made with particular attention to the exact quantitative data on the dimensions involved, and these are sometimes accompanied with extensive tabulations of these data. Perhaps the more notable of this second type of reconstructions are those of Merkel and Orr [1] (fig. 1 *a* the eye of the newborn; fig. 1 *b*, the adult eye), and Szent-Györgyi [2] (eyes of children and of adults).

One is thus provided with working quantitative data, in both numerical and graphic form, on linear and, in some instances, areal dimensions of considerable portions of the optic apparatus. Knowledge of tridimensional measures or volume or mass of optic structures is far less complete. Volume embodies in each symbol or computation an infinite number of two dimensional (infinitely thin) constructions. There are a large number of determinations of the mass and volume of the eyeball as a whole and of the lens, both at birth and in later life. The literature also contains occasional determinations of this kind of a

* Now at the Palo Alto Clinic, Department of Neurology and Psychiatry; formerly Fellow in Neurology and Psychiatry, Mayo Foundation.

‡ Graduate School, University of Minnesota.

1. Merkel, F. S., and Orr, A. W.: Das Auge des Neugeborenen an einem schematischen Durchschnitt erläutert, in Merkel, F. S., and Bonnet, R.: Anatomische Hefte, Wiesbaden, J. F. Bergmann, 1892, vol. 1, pp. 271-299.

2. Szent-Györgyi, A.: Untersuchungen über den Bau des Glaskörpers des Menschen, Arch. f. mikr. Anat. **89**:324-386, 1917.

few other optic structures, such as the cornea, the sclera and the vitreous. But there seem to be no published records of systematic efforts at estimation of the magnitudes in either mass or volume of most other portions of the eye.

DATA AND METHODS EMPLOYED IN PRESENT PAPER

The present account represents an attempt to obtain approximate values in this relatively unexplored field. The methods employed are as follows:

The material presented here is limited to the eye of the full term newborn infant and to the eye of the young adult (whenever possible, between 20 and 30 years of

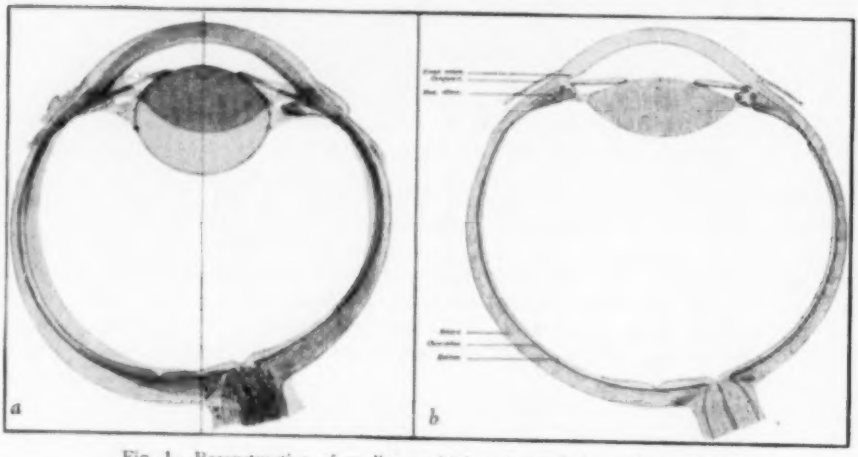

Fig. 1.—Reconstruction of median sagittal sections of the eyeball: (*a*) The eyeball at birth, after Merkel and Orr.[1] The shaded portion represents the eyeball of the adult reduced to the diameter of the eyeball of the newborn and superimposed on it. (*b*) The eyeball in maturity, after Merkel.[2]

age). The basic data used were derived in some cases from our own observations, but in the great majority of instances they were taken from previously published records. These data were assembled by a systematic survey of the literature of the subject, and they are presented in summary form in the tables of a second paper on this subject. From this tabular material we selected the values thought to be requisite to our purpose. These reference measurements are given in table 1. The key geometric formulas employed are illustrated in figure 2.

Measurement Designations.—Spatial designations in all drawings, descriptions and texts, such as "anterior," "posterior," "inferior" and "height," refer to the eyeball or its parts in the position indicated in figure 1. This is the position usually employed by anatomists, but not necessarily by ophthalmologists.

TABLE 1.—*Values Used in Present Calculations of Dimensions of the Eye*

Eye and Its Parts	Eye	
	Newborn, Mm.	Adult, Mm.
Eye as whole		
Sagittal diameter	17.5	24.4
Transverse diameter	17.1	23.8
Vertical diameter	16.5	23.5
Mean of three major diameters	17.0	23.9
Sagittal diameter, corrected *	16.7	23.5
Mean diameter, corrected †	16.8	23.6
Volume of bulb, cc.	2.4	7.7
All coats of eyeball		
Mean thickness of all coats	1.05	1.3
Cornea		
External diameter of horizontal base	10.9	11.5
External diameter of corneal arc (graphically determined)	14.0	18.2
Internal diameter of corneal arc (graphically determined)	11.9	16.4
Mean thickness	0.8	0.9
Oblique thickness (graphically determined)	1.1	1.6
Height (graphically determined)		
External	3.9	3.4
Internal	1.1	3.7
Sclera		
Mean thickness	0.7	0.9
Choroid		
Mean thickness	0.07	0.11
Height of choroid spherical zone (graphically determined) ‡	1.2	2.6
Ciliary body		
Width	2.1	4.0
Thickness	0.5	1.0
Internal diameter of bulb at periphery of ciliary body (graphically determined)	13.0	17.0
Distance between internal (lateral and medial) angles of ciliary body (graphically determined)	9.2	10.6
Iris		
Thickness	0.14	0.3
Width	2.3	4.0
Diameter at attachment (graphically determined)	9.1	....
Retina		
Mean thickness	0.38	0.5
Lens		
Anterior radius	3.7	10.0
Posterior radius	....	6.0
Height of segment in newborn, anterior chamber (graphically determined)	1.0	....
Diameter (distal) in ciliary segment (graphically determined) §	5.7	....
Diameter (proximal) in ciliary segment (graphically determined) §	6.3	....
Volume (cu. mm.)	72.0	163.0
Optic nerve (intramural portion)		
Length	1.2	1.4
Diameter (anterior)	1.2	1.8
Diameter (posterior)	2.4	3.2
Mean diameter	1.8	2.4
Anterior chamber		
Depth (graphically determined)	2.2	2.5
Depth (optically determined)	2.6	3.5
Pupil		
Mean diameter	2.5	3.5
Alternate corneal dimensions		
Cornea, thickness at vertex (observed)	0.8	1.0
Cornea, thickness at margin	1.0	1.1

* This correction of the sagittal diameter is made to modify the increased length of this diameter, owing to the anterior bulge of the cornea. The bulge of the corneal segment distorts the true arc subtending the sagittal diameter.

† The corrected mean diameter is the corrected sagittal diameter in determination of the mean diameter of the optic bulb.

‡ Height of choroid spherical zone, graphically determined, is the segment of the bulbar portion of the eye occupied by the ciliary body. The measurable choroidal shell does not occupy the entire bulbar segment, as does the sclera. In this determination, it is necessary to subtract a portion of the volume of the ciliary body according to calculation 4, given in the text.

§ Measurements of the distal and proximal diameters of the segment of the lens that projects into the ciliary segment are necessary for the determination of the volume of the lens in the calculation of the volume of the posterior chamber. Determinations were made in reference figures 1 and 2. The height of the segment of the lens between the ares in the eye of the newborn infant is 0.57 mm.

Reference Measurements.—The necessary selection involves some subjective factors. In many instances, average values based on the determinations of a variable number of observations seemed sufficient. But in certain others, averages were not enough, for the validity of the published figures obviously varied with the number of observations and the technics of observation employed and the detail of supporting data given by the several observers. The values selected in these instances, therefore, are considered only judgments. It is unlikely that they would be entirely duplicated by other investigators reviewing the same data, although we think that the divergences in choice would be relatively few and slight.

Some fourteen reference measurements or calculations were not available from our own observations or from the data lists; these were obtained by measurements of the carefully scaled reconstructions of Merkel [3] and Merkel and Orr.[1] These graphic observations were made with great care, with use of a fine metal rule calibrated to 0.5 mm.; a fine-pointed steel engineer's divider, and a magnifying glass were necessary.

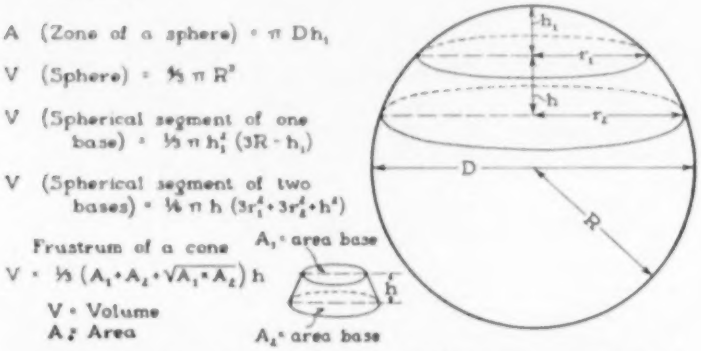
A (Zone of a sphere) = π D h₁
V (Sphere) = ⅔ π R³
V (Spherical segment of one base) = ⅓ π h₁² (3R - h₁)
V (Spherical segment of two bases) = ⅙ π h (3r₁² + 3r₂² + h²)
Frustrum of a cone
V = ⅓ (A₁ + A₂ + √A₁ × A₂) h
V = Volume
A = Area
A₁ = area base
A₂ = area base
h₁
r₁
h
r₂
D
R
h

Fig. 2.—Key geometric formulas used in approximating the volume of optical structure. *A* is the area of a zone of a sphere; *V*, the volume of a sphere and spherical segments of one base and of two bases, and the volume of the frustum of a cone.

These selected data were next used in a series of geometric constructions. The form of the eye as a whole, as well as that of many of its component parts, may be approximated by certain simple geometric figures. These geometric figures include spheres; spherical segments, both of one base and of two bases; cylinders; frustums of cones; spherical shells, and a prismatic ring. It is improbable that the forms, and therefore the volumes, of the various ocular parts are ever exact duplicates of the geometric figures that they approximate. However, at a number of steps in the calculation it has been possible to check values obtained by geometric calculations against observed values, and the differences ranged from 5 to 10 per cent.

The lens, which easily can be removed in toto, has been the subject of a number of reliable volumetric studies. A geometric formula for calculation of the volume

3. Merkel, F.: Handbuch der topographischen Anatomie: Zum Gebrauch für Aerzte, Braunschweig, F. Vieweg und Sohn, 1885, vol. 1, p. 239.

of the lens would be complicated, and perhaps questionable, and would add nothing. Therefore, we have not included the lens in our geometric calculations but have used observed values of its volume. We have calculated the volume of the remaining components of the eyeball, a few of which might possibly be removed and measured directly with great difficulty, while others probably could not be measured at all in this manner. For example, although the cornea might be removed and its volume ascertained, it is doubtful whether the choroid, sclera or retina would lend themselves to direct handling without the introduction of gross experimental error. The same is true of the intramural portion of the optic nerve, the ciliary body, the iris and the various chambers of the eyeball.

It was necessary to make certain assumptions which, although they are not strictly true, conform so closely to reality that the error thus introduced is reasonably small. For example, we have assumed that the corneal surfaces are perfectly spherical with different radiuses. This permits the use of a simple formula. Actually, the widening base of the cornea could be taken into account, but this would imply a higher degree of precision and accuracy of the original measurements than they probably represent.

The eyeball is assumed to be a sphere, and its coats are regarded as of uniform thickness, although this is not strictly true. The error was minimized by the use of mean figures from several measurements and correction for the anterior corneal bulge of the eyeball.

In addition to discrepancies that occur in the computations as a result of some nonconformity of geometric form and the natural form of objects, there is another source of error that can only be estimated. This is the gratuitous variability that occurs in all quantitative determinations of natural structures. Optical structures, however, show a small variability as compared with that of most other structures of the body. The coefficients of variability of the optical structures in the newborn is greater than that of the adult person, probably because of the inclusion of observations on premature infants with those on full term newborn infants. Discrepancies arising from this normal natural variability cannot be eliminated from the results of calculations made in the manner here described.

The geometric approach here followed requires the use of a number of approximations and includes the possibility of the introduction of error through certain geometric assumptions, but it has the advantage of permitting the use of precise and uniform methods in the quantitative analysis of a large amount of varied data. Furthermore, it permits the simplicity of mathematical expression that is always useful in morphologic studies.

To quote from Sir D'Arcy Wentworth Thompson's [4] classic study: "The study of form may be descriptive merely, or it may become analytical. We begin by describing the shape of an object in simple words of common speech: we end

4. Thompson, D'A. W.: On Growth and Form, New York, Cambridge, University Press, 1917.

by defining it in the precise language of mathematics; the one method tends to follow the other in strict scientific order and historical continuity. . . . The mathematical definition of a 'form' has a quality of precision which was quite lacking in our earlier stage of mere description; it is expressed in few words, or in still briefer symbols, and these words or symbols are so pregnant with meaning that thought itself is economised; we are brought by means of it in touch with Galileo's aphorism, that 'the Book of Nature is written in characters of Geometry.'"

CALCULATIONS

CALCULATION 1: *Volume of the Eyeball.*—Values used in the present calculations are found in table 1.

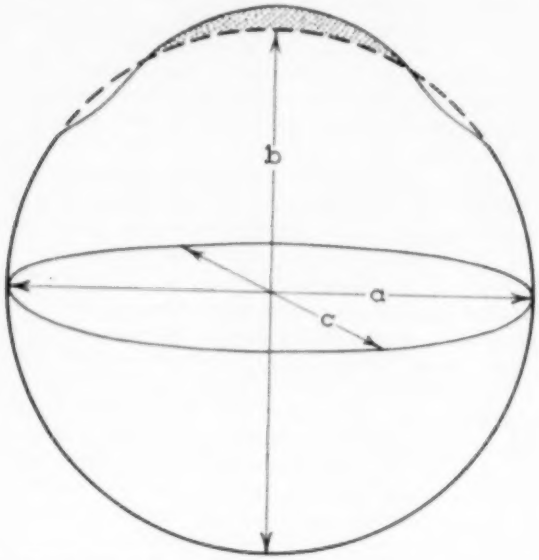

Fig. 3.—The human eyeball considered as a sphere. *a*, *b* and *c* are transverse, corrected sagittal and vertical diameters, respectively. The broken line represents the corrected anterior arc of the sagittal plane of the eyeball after modification for the anterior extension of the cornea.

Volume of the eyeball is first calculated on the assumption that the eye is a perfect sphere. The average of the vertical transverse and the sagittal radiuses is used (fig. 3). It is necessary to correct for the anterior bulge of the corneal segment, which gives the sagittal diameter an excessive length. This correction is experimentally determined by swinging a pair of dividers. A corrected sagittal diameter is estimated by establishing an arc across the base of the corneal

segment with dividers set with one leg at the geometric center of the optic bulb and the other at any given point on the external surface of the sclera (fig. 1). The apex of the arc thus established passes through the inner margin of the cornea at its apex. This new diameter is averaged with the other two, and the usual geometric formulas for the volume of a sphere (see figure 2 for this and succeeding formulas) are employed.

Calculation 1, of the volume of the eyeball considered as a perfect sphere, is as follows: $V = 4/3 \pi R^3$

For the adult eyeball this becomes

$$V = 4.189 \times \left(\frac{23.6}{2}\right)^3 = 6,882.3 \text{ mm.}^3$$

For the eyeball of the newborn this becomes

$$V = 4.189 \times \left(\frac{16.8}{2}\right)^3 = 2,482.7 \text{ mm.}^3$$

CALCULATIONS 2, 3 and 4: *Volume of the Eyeball.*—As a matter of fact, the eye consists of not one sphere but, rather, of approximate segments of two spheres. A minor segment of a small sphere, representing the cornea, rests on a major segment of a larger sphere, representing the eyeball proper. This geometric construction is illustrated by figure 4.

The basis of further calculation of the bulbar and corneal segments of the eye, as well as all the coats of the eyeball and the anterior chamber, is the usual geometric formula for the volume of a segment of a sphere.

Calculation 2: The volume of the bulbar segment is the volume of a major segment of a sphere, since it represents the larger portion of the sphere, in contrast to the volume of the corneal segment, which is the minor portion of a different, and a smaller, sphere. The height of the bulbar segment, which is necessary for this calculation, is the sagittal diameter of the eyeball less the corneal height which was graphically observed. The radius, of course, is half the corrected mean diameter.

The volume of the corneal segment is similarly determined. Its height is graphically determined from the enlarged standard figures of Merkel [3] and Merkel and Orr.[4] The radius is half the diameter of a circle the arc of which is identical with that of the cornea (graphically determined external diameter of the corneal arc).

The calculated volume of the eyeball is next determined simply by adding the bulbar and the corneal segment.

Calculation 2, of the volume of the bulbar segment (major segment of a sphere), is as follows:

$$V = \tfrac{1}{3} \pi h^2 (3R - h)$$

For the adult eyeball this becomes

$$V = 1.0472 \times (24.4 - 3.4)^2 \times [3 \times (\tfrac{24.4}{2}) - (24.4 - 3.4)] = 6{,}650.1 \text{ mm.}^3$$

For the eyeball of the newborn this becomes

$$V = 1.0472 \times (16.7 - 3)^2 \times [3 \times (\tfrac{16.7}{2}) - (16.7 - 3)] = 2{,}260.3 \text{ mm.}^3$$

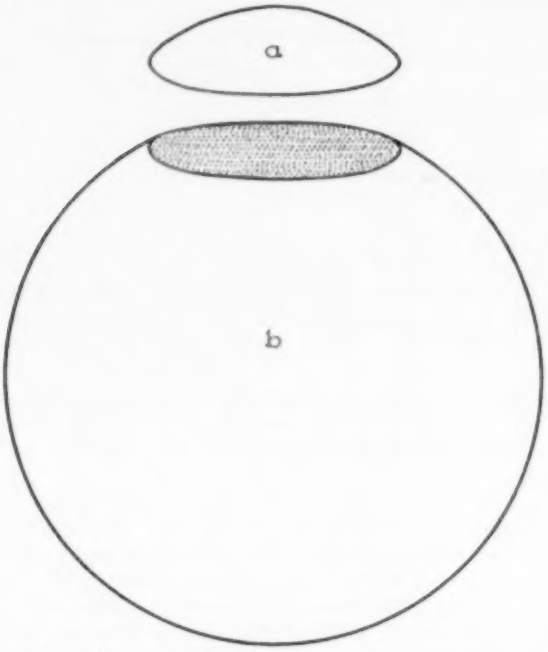

Fig. 4.—Geometric construction illustrating the division, for purposes of calculation, of the eyeball into (*a*) an anterior, or corneal, segment, and (*b*) a posterior, or bulbar, segment.

Calculation 3, of the volume of a corneal segment (minor segment of a sphere), is as follows:

$$V = \tfrac{1}{3}\,\pi\,h^2\,(3R - h)$$

For the adult eyeball this becomes

$$V = 1.0472 \times (3.4)^2 \times [3 \times (\tfrac{10.2}{3}) - 3.4] = 289.4 \text{ mm.}^3$$

For the eyeball of the newborn this becomes

$$V = 1.0472 \times (3)^2 \times [3 \times (\tfrac{14}{6}) - 3] = 169.7 \text{ mm.}^3$$

Calculation 4, calculated corrected volume of the eyeball (volume of a major segment of a sphere [calculation 2] plus volume of a minor segment of a sphere [calculation 3]), becomes
For the adult eyeball

$$V = 6{,}650.14 + 289.43 = 6{,}939.6 \text{ mm.}^3$$

For the eyeball of the newborn

$$V = 2{,}260.3 + 169.7 = 2{,}430.0 \text{ mm.}^3$$

CALCULATION 5: *Volume of the Sclera.*—The coats of the eye in the bulbar segment include the sclera, the choroid and the retina, which

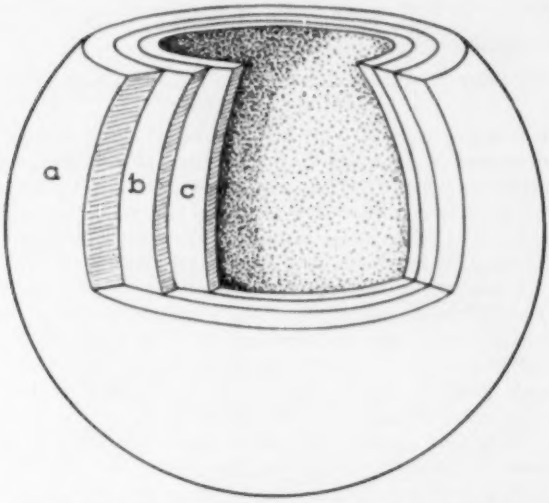

Fig. 5.—Geometric construction illustrating the division, for the purpose of calculation, of the coats of the bulbar segment of the eyeball into three successive concentric shells: (*a*) scleral; (*b*) choroidal; (*c*) retinal.

may be considered as three concentric spheroidal shells of different thicknesses (fig. 5). Since the volume of the bulbar segment has already been determined, we next calculate the volume of a major segment of a sphere the diameter of which is equal to the diameter of the bulbar segment minus twice the thickness of the sclera. The height of this major segment of the sphere equals the height of the bulbar segment less the thickness of the sclera. We shall term the smaller sphere the "inner scleral sphere," although it may equally well be called the "outer choroidal sphere." When the volume of this major segment of a sphere is subtracted from the volume of the bulbar segment, the

remainder is the volume of the sclera. A very minor correction is made by subtracting the volume of the portion of the sclera occupied by the optic nerve.

Calculation 5, volume of the sclera (volume of the bulbar segment of a sphere [calculation 2] minus volume of the inner scleral sphere minus correction for volume of the scleral portion of the optic nerve [calculation 10]), is as follows:

$$V \text{ (volume of inner scleral sphere)} = \tfrac{1}{3}\pi h^2 (3R - h)$$

For the adult eyeball this becomes

$$V = 1.0472 \times (23.6 - 3.4 - 0.9)^2 \times [3(\tfrac{23.6 - 3.8}{2}) - (23.6 - 3.4 - 0.9)]$$
$$- 5,227.0 - 7.3 = 1,415.7 \text{ mm.}^3$$

For the eyeball of the newborn this becomes

$$V = 1.0472 \times (16.8 - 3 - 0.7)^2 \times [3 \times (\tfrac{16.8 - 1.4}{2}) - (16.8 - 3.7)]$$
$$- 1,797.1 - 3.2 = 460.0 \text{ mm.}^3$$

Calculation 6: *Volume of the Choroid.*—Volume of the choroid is approximated by subtraction of the volume of the inner choroidal sphere from the volume of the inner scleral sphere. A correction is made for the intramural portion of the optic nerve which passes through the choroid. The height of the choroidal sphere equals the height of the bulbar segment less the thickness of both sclera and choroid. The radius equals the diameter of the bulbar segment less twice the thickness of sclera and choroid divided by 2, or the radius of the bulbar segment less both the sclera and the choroid. It is necessary to make an additional correction of this approximate value, for, unlike the sclera, the choroid does not extend completely to the anterior margin of the bulbar segment as a distinct and measurable layer. In fact, it extends only to the inferior border of the ciliary body, with which it is indistinguishably merged. We have called this element the "spherical zone of the choroid." This is illustrated in figure 6. As will be seen in this figure, the spherical zone of the choroid is to be subtracted from the entire choroidal segment to obtain a corrected value. The ciliary body rests directly on the sclera in the area of the choroidal zone.

Calculation 6, of the volume of the choroid (volume of the major segment of the scleral sphere [calculation 5] minus volume of the major segment of the choroidal sphere with correction for volume of the choroidal spherical segment [calculation 7] and correction for volume of the choroidal part of the optic nerve [calculation 9], is as follows:

$$V \text{ (major choroidal segment of sphere)} = \tfrac{1}{3}\pi h^2 (3R - h)$$

For the adult eyeball this becomes

$$V = 1.0472 \times (23.6 - 3.4 - 0.9 - 0.11)^2 \times [3 \times (\tfrac{23.6 - 2.62}{2}) - (23.6 - 4.41)]$$
$$= 5,082.74$$

$$V = 5,226.94 - 5,082.74 - 11.07 - 0.5 = 132.1 \text{ mm.}^3$$

For the eyeball of the newborn this becomes

$$V_s = 1.0472 \times (16.8 - 3 - 0.7 - 0.07)^2 \times [3 \times (\tfrac{18.8 - 1.51}{2}) - (16.8 - 3 - 0.7 - 0.07)] = 1,753.0$$

$$V = 1,797.1 - 1,753.0 - 0.179 - 3.2 = 40.7 \text{ mm.}^3$$

CALCULATION 7: *Choroidal Correction.*—A correction for the choroidal spherical segment is made by assuming that there is a segment of a sphere with two bases the height of which is the perpendicular height of this segment, as shown in figure 6. By use of the geometric formula for a spherical segment with two bases, it is possible to compute two spherical segments: an outer and an inner.

The radius of the superior surface of the outer spherical segment is obtained by subtracting the oblique thickness of the cornea at its base

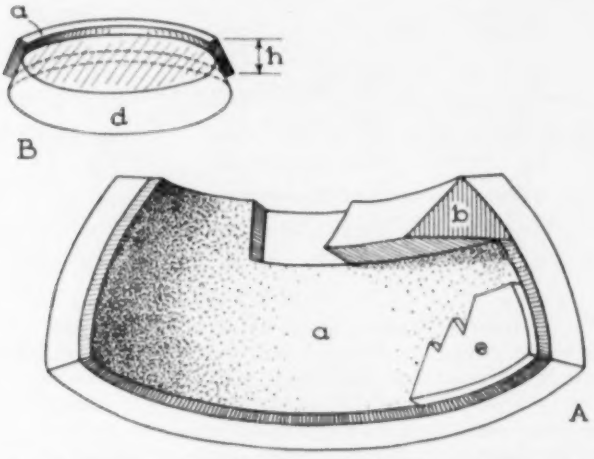

Fig. 6.—Geometric reconstruction illustrating the method of correction of the preliminary calculated volume of the choroidal coat. This correction involves the subtraction of the value of an assumed anterior ring equal in height to the lateral surface of the ciliary body. It is made by computing a value equal to the volume of an outer shell of a spherical segment with two bases. The diameter of the minor base is equal to the distance between the anterior lateral margins of the ciliary body. The diameter of the major base is equal to the distance between the posterior lateral margins of the ciliary body. The height of the segment is equal to the lateral height of the ciliary body, and the thickness of the shell is the thickness of the choroid used in the computation of the first approximation of the volume of this structure.

A, cut-away view of the segment of the eye illustrating the choroid (*a*) and its hypothetic extension to the anterior margin and a part of the ciliary body (*b*) in its true position; retina (*e*) cut away.

B, geometric reconstruction, showing method of determination of the volume of the assumed anterior ring of the choroid for the purpose of subtraction from the preliminary approximation of the volume of the choroid. (*a*) The hypothetic anterior ring of the choroid coat assumed to be present for the preliminary calculation of the volume of this coat; (*h*) height of the assumed ring; (*d*) volume of the core of the case of the spheroidal segment with two bases.

from the external diameter (or horizontal base) of the cornea. These measurements of the base of the cornea are also those of the superior surface of the bulbar segment.

The radius of the inferior surface of the outer spherical segment is obtained by adding twice the thickness of the choroid to the graphically determined internal diameter of the bulb at the periphery of the ciliary body and dividing by 2. In this way, the sclera is eliminated from the calculations, as shown in the cross section drawing in figure 6. The final step is the elimination of the inner segment, which leaves the volume of the choroid desired.

Calculation 7, of the choroidal correction (volume of the outer spherical segment with two bases — volume of inner spherical segment with two bases), is as follows:

$$V = V_1 - V_2$$
$$V = 1/6\,\pi\,h\,(3r^2_1 + 3r^2_2 + h^2) - 1/6\,\pi\,h\,(3r^2_3 + 3r^2_4 + h)$$

For the adult eyeball this becomes

$$V_1 = 0.5236 \times 2.6 \times [3 \times \left(\tfrac{11.8 - 2.2}{2}\right)^2 + 3 \times \left(\tfrac{17.0 + 0.22}{2}\right)^2 + 2.6^2] = 387.08$$

$$V_2 = 0.5236 \times 2.6 \times [3 \times \left(\tfrac{11.8 - 2.2 - 0.22}{2}\right)^2 + 3 \times \left(\tfrac{17}{2}\right)^2 + 2.6^2] = 376.01$$

$$V_1 - V_2 = 11.07 \text{ mm.}^3$$

For the eyeball of the newborn this becomes

$$V_1 = 0.5236 \times 1.2 \times [3 \times \left(\tfrac{10 - 2.2}{2}\right)^2 + 3 \times \left(\tfrac{13 + 0.14}{2}\right)^2 + 1.2^2] = 110.95$$

$$V_2 = 0.5236 \times 1.2 \times [3 \times \left(\tfrac{10.0 - 2.2 - 0.14}{2}\right)^2 + 3 \times \left(\tfrac{13}{2}\right)^2 + 1.2^2] = 108.19$$

$$V_1 - V_2 = 2.76 \text{ mm.}^3$$

CALCULATION 8: *Volume of the Retina.*—Retinal volume is computed by subtracting the volume of the inner retinal segment from the volume of the inner choroidal segment with an appropriate correction for the optic nerve. Attempts to calculate the retinal volume involved in the numerous foldings of the pars ciliaris retinae proved impracticable and were abandoned. The pars iridica retinae, or that portion of the retina on the posterior surface of the iris, was included with the iris, since it is structurally and functionally quite distinct from the optical portion. We estimate that the volume of the pars iridica retinae in the adult eyeball is approximately one-fifth to one-fourth the volume of the iris.

Calculation 8, of the retinal volume (volume of the choroidal segment sphere [calculation 6] minus volume of the retinal segment sphere, with correction for retinal optic nerve [calculation 9]), is as follows:

$$V \text{ (volume retinal sphere)} = \tfrac{1}{3}\,\pi\,h^2\,(3R - h)$$

For the adult eyeball this becomes

$$V = 1.0472\,(23.6 - 3.4 - 0.9 - 0.11 - 0.3)^2 \times [3 \times \left(\tfrac{23.6 - 3.02}{2}\right) - (23.6 - 3.4 - 0.9 - 0.11 - 0.3)] = 4,700.77$$

$$V = 5,082.74 - 4,700.77 - 0.60 = 381.4 \text{ mm.}^3$$

For the eyeball of the newborn this becomes

$$V_s = 1.0472 \times (16.8 - 3 - 0.7 - 0.07 - 0.28)^2 \times [3 \times (\tfrac{16.8 - 1.54 - 0.98}{2}) - (16.8 - 3 - 0.7 - 0.07 - 0.28)] = 1{,}583.14$$

$$V = 1{,}753.05 - 1{,}583.14 - 0.3 = 169.7$$

CALCULATIONS 9 and 10: *Volume and Fractions of the Volume of the Intramural Portion of the Optic Nerve.*—The intramural portion of the optic nerve perforates the posterior pole of the optic bulb as a truncated cone, or frustum of a cone, being largest posteriorly, much like a cork plugged into a cask (fig. 7). This part of the nerve can be divided into scleral, choroidal and retinal portions.

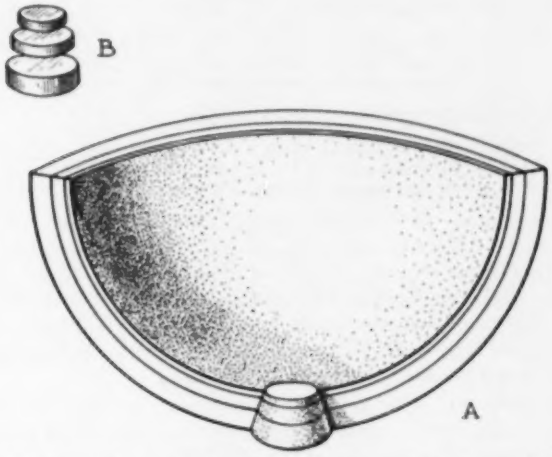

Fig. 7.—Geometric constructions illustrating the method of correction of the calculated volumes of the several coats of the bulbar segment of the eyeball by subtraction of the particular portion in each coat occupied by the optic nerve. *A*, schematic diagram of the position and space occupied by the optic nerve; *B*, schematic diagrams of the three cylindric volumes subtracted for correction of values for the retina, choroid and sclera, respectively.

The volume of the scleral, choroidal and retinal portions could be determined as successive frustums of a cone, but this would require additional and questionable estimates of the thickness of these three coats in the region of entrance of the optic nerve. We have, therefore, calculated these three nerve segments as simple cylinders, each having the mean radius of its nerve cone segment and the height of the mean thickness of the layer in question. The error introduced by this form of calculation is so small as to be entirely negligible.

Calculation 9, of the volume of the intrabulbar portion of the optic nerve (truncated cone), is as follows:

$$V = \tfrac{1}{3}\,(\tfrac{1}{4}\,\pi\,D^2_1 + \tfrac{1}{4}\,\pi\,D^2_2 + \sqrt{\tfrac{1}{4}\,D^2_1 \times \tfrac{1}{4}\,D^2_2}) \times h$$

For the adult eyeball this becomes

$$V = \tfrac{1}{3}\,(0.7854 \times 1.6^2 + 0.7854 \times 3.2^2 + \sqrt{1.6384}) \times 1.4 = 5.3\ \text{mm.}^3$$

For the eyeball of the newborn this becomes

$$V = \tfrac{1}{3}\,(0.7854 \times 1.2^2 + 0.7854 \times 2.4^2 + \sqrt{0.5184}) \times 1.2 = 2.5\ \text{mm.}^3$$

Calculation 10, of fractions of the volume of the intrabulbar portion of the optic nerve (volume of a cylinder), is as follows:

$$V = \pi\,R^2\,h$$

For the adult eyeball this becomes

Scleral portion: $3.1416 \times 1.6^2 \times 0.9 = 7.30$
Choroidal portion: $3.1416 \times 1.2^2 \times 0.11 = 0.50$
Retinal portion: $3.1416 \times 0.8^2 \times 0.3 = 0.60$

For the eyeball of the newborn this becomes

Scleral portion: $3.1416 \times 1.2^2 \times 0.7 = 3.20$
Choroidal portion: $3.1416 \times 0.9^2 \times 0.07 = 0.20$
Retinal portion: $3.1416 \times 0.6^2 \times 0.28 = 0.30$

Calculation 11: *Volume of the Cornea.*—Corneal volume is estimated by subtracting the volume of the inner corneal segment from the volume of the corneal segment as a whole, as previously determined.

The inner and outer corneal surfaces are arcs of somewhat different circles, as shown in figure 8. The radius of the inner corneal segment was graphically determined; its height equals the observed corneal height less the mean corneal thickness.

Calculation 11, of the volume of the cornea (volume of the corneal segment [calculation 3] minus volume of the inner corneal segment), is as follows: $V\ (\text{inner corneal segment}) = \tfrac{1}{3}\,h^2\,(3R - h)$

For the adult eyeball this becomes

$$V_s = 1.0472\ (3.4 - 0.9)^2 \times [3 \times (\tfrac{16.4}{2}) - 2.5] = 144.65$$
$$V = 289.43 - 144.65 = 144.8$$

For the eyeball of the newborn this becomes

$$V = 1.0472 \times (3 - 0.8)^2 \times [3 \times (\tfrac{11.8}{2}) - (3 - 0.8)] = 72.48$$
$$V = 169.65 - 72.48 = 97.2\ \text{mm.}^3$$

Calculation 12: *Volume of the Iris.*—The iris may be regarded as a short, broad cylinder containing the pupil. The pupil is also a spatial cylinder, the volume of which when subtracted from the combined volume of the iris and the pupil, which for practical geometric purposes are calculated together, gives the volume of the iris. Although these structures are not conventional geometric objects, they closely approximate them (fig. 9).

The iris, of course, is a body of functionally changing size. We have limited our calculations to its volume in the neutral state.

Calculation 12, of the volume of the iris (volume of the cylinder minus volume of the enclosed cylinder), is as follows:

$$V = A_1 \times h - A_2 \times h = \pi r^2_1 h - \pi r^2_2 h$$

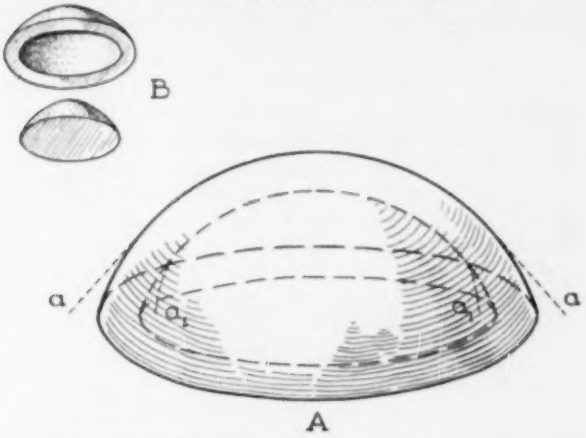

Fig. 8.—Geometric constructions illustrating the division of the anterior, or corneal, segments of the eyeball for the purpose of calculation. *A*, the geometric construction of the corneal segment; *a* and *a'* represent the correction introduced for the thickening of the cornea at its base. *B*, divisions of the corneal segment in the corneal shell and the anterior chamber.

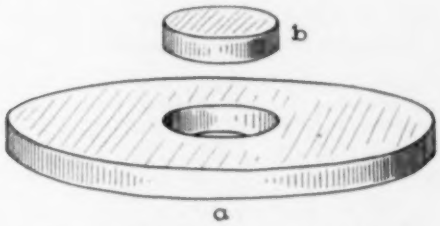

Fig. 9.—Geometric construction of the iris as a cylindric plate, with correction for the pupil, with the eye at rest, by the subtraction of a small central cylindric position. *a* is the iris; *b*, the pupil.

For the adult eyeball this becomes

$$V = [3.1416 \times (1.75 + 4)^2 \times 0.3] - [3.1416 \times 1.75^2 \times 0.3]$$
$$V = 31.16 - 2.88 = 28.3 \text{ mm.}^3$$

For the eyeball of the newborn this becomes

$$V = [3.1416 \times 4.55^2 \times 0.14] - [3.1416 \times (\tfrac{9.1 - 6.9}{2})^2 \times 0.14]$$
$$V = 9.10 - 0.69 = 8.4 \text{ mm.}^3$$

CALCULATION 13: *Volume of the Ciliary Body.*—Reduction of the ciliary body to a simple geometric figure is somewhat difficult, and perhaps a little questionable. The ciliary body in its normal position

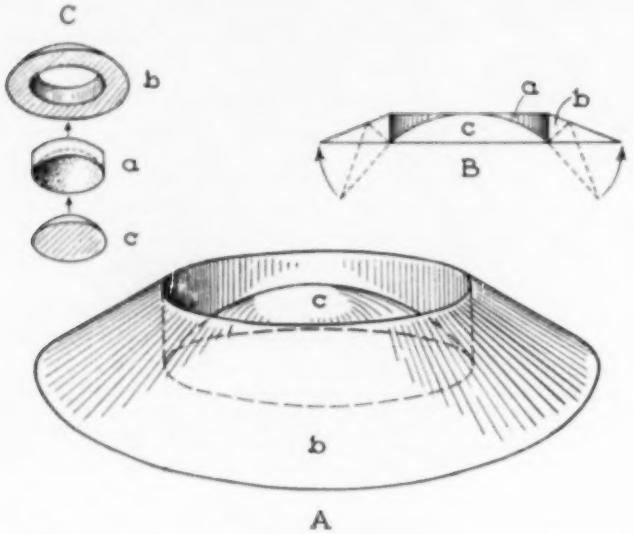

Fig. 10.—Geometric constructions used in computing the approximate volume of the ciliary body.

A, a tridimensional view of an approximation of the ciliary body considered as a three-sided prismatic ring. The area extending forward in the middle portion of this figure represents the border of the anterior surface of the lens.

B, the same construction seen in transection. The triangles, indicated by broken lines, represent cross sections of the ciliary body in their approximate anatomic position. The geometric constructions are rotated on their posterior internal angles through about 30 degrees to establish parts of the base of a truncated cone, artificially eliminating space, *b*. This rotation affects neither the area of the triangles nor the calculated volume of the ring. The shaded areas are approximate cross sections of the uncorrected posterior chamber of the eye. The central, unshaded area, *c*, is a cross section of that portion of the lens extending forward between the medial borders of the ciliary body, and the shaded portion, *a*, is the posterior chamber.

C, division of the construction of the ciliary region into three geometric components: (*a*) a central cylinder, representing an approximation of the space occupied by the posterior chamber and a portion of the anterior part of the lens; (*b*) the ciliary body considered as a prismatic, ring-shaped portion of the frustum of a cone; (*c*) the anterior portion of the lens bounded laterally by the posterior chamber.

does not conform perfectly to any simple geometric body. However, its volume at least approximates that of a geometric figure that is a right-angled triangular body in cross section and circular in contour (fig. 10). The hypotenuse of this triangle is that portion of the ciliary body that lies in contact with the sclera. To transform the ciliary body, thus assumed, it is necessary to rotate the triangle on its medial and inferior angle until its base lies on a straight line perpendicular to the sagittal axis of the eye (fig. 10). Such rotation does not, of course, change either the form or the area of the triangle.

Thus, the ciliary body so rearranged forms, together with the enclosed cylinder, a truncated cone. This truncated cone has a superior surface, the radius of which equals one-half the graphically observed distance between the internal (lateral and medial) angles of the ciliary body. The radius of the base, which is graphically determined, equals the radius of the enclosed cylinder (or superior surface) plus the length of the base of the triangular ciliary body in cross section. The height of the cone is the height of the medial side of the triangular segment of the ciliary body. Various components and features can be seen in tridimensional form in figure 10.

CALCULATION 13, volume of the ciliary body (volume of the frustum of a cone minus volume of an enclosed cylinder), is as follows:

$$V = \tfrac{1}{3}\left(\pi r^2_1 + \pi r^2_2 + \sqrt{\pi r^2_1 \times \pi r^2_2}\right) h - \pi r^2_1 h$$

For the adult eyeball this becomes

$$V = \tfrac{1}{3}\left(3.1416 \times 5^2 + 3.1416 \times 8^2 + \sqrt{3.1416 \times 5^2 \times 3.1416 \times 8.0^2}\right) \times 1 - (3.1416 \times 5^2 \times 1) = 56.6 \text{ mm.}^3$$

For the eyeball of the newborn this becomes

$$V = \tfrac{1}{3}\left(3.1416 \times 4.6^2 + 3.1416 \times 6.7^2 + \sqrt{3.1416 \times 4.6^2 \times 3.1416 \times 6.7^2}\right) \times 0.5 - (3.1416 \times 4.6^2 \times 0.5) = 17.5 \text{ mm.}^3$$

CALCULATIONS 14 and 15: *Volume of the Anterior Chamber.*—The volume of the anterior chamber is computed by subtracting the volume of the iris from the volume of the inner segment of the corneal sphere. The height and radiuses are graphically determined. In the case of the newborn eye, as indicated by Merkel [5] and by von Hippel,[5] the lens actually projects into the anterior chamber. Thus, the anterior chamber of the eye of the newborn is reduced by the volume of that portion of the lens projecting into it. This correction is employed in the alternate calculation of the volume of the anterior chamber in the newborn. The height and radius are graphically determined.

5. von Hippel, E.: Ueber das normale Auge des Neugeborenen, Arch. f. Ophth. **45**:286-312, 1898.

Calculation 14, of the volume of the anterior chamber (volume of the inner corneal segment in a sphere [calculation 10] minus volume of the iris [calculation 11]), is as follows:

For the adult eyeball this becomes

$$V = 144.65 - 28.28 = 116.4 \text{ mm.}^3$$

For the eyeball of the newborn this becomes

$$V = 72.48 - 8.41 = 64.1 \text{ mm.}^3$$

An alternate calculation (volume of the anterior chamber, with correction for lens projecting into anterior chamber [calculation 15]), is as follows:

$$V = 64.07 - 6.9 = 57.17$$

Calculation 15, the correction for a segment of the lens sphere projecting into the anterior chamber of the eyeball of the newborn, is as follows:

$$V = \tfrac{1}{3}\, h\, (3R - h)$$
$$V = 1.0472 \times 0.8^2 \times (3 \times 3.7 - 0.8)$$
$$V = 1.0472 \times 0.64 \times 10.3 = 6.9$$

Calculations 16 and 17: *Volume of the Posterior Chamber.*—The schematic geometric form of the posterior chamber is illustrated in figure 11. The cross section drawing is in keeping with figure 10 *B*, which illustrates the rotation of the ciliary body which is necessary to obtain a geometric calculation for that component. We are aware that, in performing this rotation, the volume of the posterior chamber is slightly reduced. The change is not great, and we have chosen to calculate all the components in one assumed position rather than to establish a special case for each component, a practice which would entail more complicated formulas and would imply a degree of precision not possible to attain on the basis of the data and the determinations.

Since the volume of the enclosed cylinder has already been determined, we subtract the volume of that segment of the lens projecting into the so-called enclosed cylinder (fig. 11). The remaining portion of the cylinder is the posterior chamber plus a small part of the zonule of Zinn. The radiuses and the height of the lens segment are graphically determined.

As already noted in the case of the eyeball of the newborn infant, the lens may project into the anterior chamber. Therefore, an alternate calculation is necessary to correspond with the alternate calculation of the volume of the anterior chamber. In this calculation, that portion of the volume of the lens lying in the intraciliary body cylinder is determined as a spherical segment with two bases. The inferior base is the same as that used in the calculation of the volume of the enclosed cylinder, while the superior base is the same as the inferior base of the segment of the lens sphere in the alternate calculation of the volume of the anterior chamber.

Calculation 16, volume of the posterior chamber and part of the zonule (volume of the enclosed cylinder in truncated cone of the ciliary body [see calculation 12] minus volume of the enclosed lens), is as follows:

$$V \text{ (minor segment of enclosed lens of sphere)} = \tfrac{1}{3}\,\pi\,h^2\,(3R - h)$$

For the adult eyeball this becomes

$$V = 1.0472 \times 1^2 \times \left[3 \times \left(\tfrac{10}{6}\right) - 1\right] = 14.66$$
$$V = 78.54 - 14.66 = 63.9 \text{ mm.}^3$$

For the eyeball of the newborn this becomes

$$V = 1.0472 \times 0.5^2 \times (3 \times 3.7 - 0.5) = 2.78$$
$$V = 33.20 - 2.78 = 30.4 \text{ mm.}^3$$

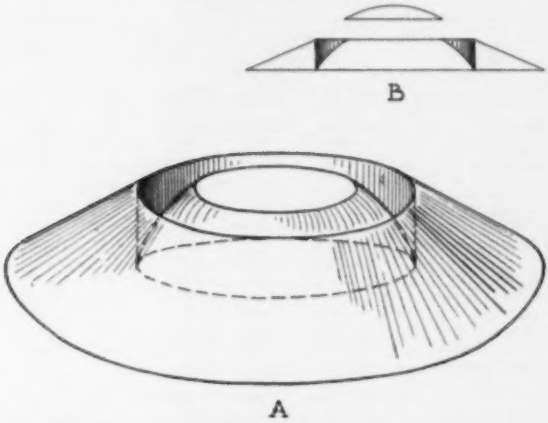

Fig. 11.—Geometric reconstructions made to determine the volume of the posterior chamber, illustrating an alternate calculation of the volume of the posterior chamber of the eye. In this instance, the anterior surface of the lens is assumed to project forward a little into the anterior chamber, a condition frequently illustrated in sections of the median plane of the eye of the newborn infant. In this calculation, the form of the portion of the lens bounded laterally by the posterior chamber is approximated by a spherical segment with two bases.

Alternate calculation 17, of the volume of the posterior chamber and part of the zonule in the eye of the newborn (volume of enclosed cylinder in truncated cone of ciliary body [calculation 12] minus volume of enclosed lens calculated as spherical segment with two bases), is as follows:

$$V = 1/6 * h\,(3r^2_1 + 3r^2_2 + h^2)$$

For the eyeball of the newborn this becomes

$$V_1 = 1/6 \times 3.1416 \times 0.5\,([3 \times 2.9^2] + [3 \times 3.2^2] + 0.5^2) = 14.7$$
$$V = 33.2 - 14.7 = 18.5 \text{ mm.}^3$$

CALCULATIONS 18 and 19: *Area of the Anterior Corneal Surface and Area of Anterior Retinal Surface.*—The area of the anterior surface of the cornea is determined as a zone of a segment of a sphere.

We have found no reliable published estimates of the retinal area. The same formula for the areas of a zone of a sphere is employed. The diameter equals the corrected average diameters of the bulb, less twice the mean thickness of the sclera, choroid and retina. The height equals the same diameter less the graphically observed corneal height, less the sum of the mean thicknesses of the three coats.

TABLE 2.—*Computed Values of Structures and Spaces of the Eyeball*

Structures and Spaces	Values for Newborn		Values for Adults		Values for Adults as Multiples of Values for Newborn	Changes in Percentage Values from Birth to Maturity
	Absolute, Cu. Mm.	Percentage of Eyeball	Absolute, Cu. Mm.	Percentage of Eyeball		
Entire eyeball	2,430.0	100.00	6,909.6	100.00	2.86	.....
Corneal segment	169.7	6.98	289.4	4.17	1.70	−2.81
Bulbar segment	2,260.3	93.02	6,620.1	95.83	2.94	+2.81
Combined volume of all structural components	809.3	33.77	2,336.9	33.67	2.69	−2.10
Combined volume of all humoral components	1,360.7	64.23	4,765.7	68.67	3.05	+4.44
Combined volume of all coats	797.3	32.81	2,173.9	31.33	2.73	−1.48
Sclera	460.6	18.93	1,416.0	20.41	3.10	+1.61
Cornea	97.2	4.00	144.8	2.09	1.49	−1.91
Choroid	40.7	1.68	132.1	1.90	3.22	+0.22
Retina	169.7	6.98	381.4	5.50	2.25	−1.47
Ciliary body	17.5	0.72	56.6	0.81	3.23	+0.10
Iris	8.6	0.35	28.5	0.40	3.27	+0.15
Intramural portion of optic nerve	2.5	0.10	5.3	0.08	2.08	−0.03
Lens	72.0	2.96	163.0	2.35	2.26	−0.61
Anterior chamber	64.1	2.64	116.4	1.68	1.82	−0.96
Posterior chamber plus part of zonule	30.4	1.25	68.9	0.99	2.10	−0.23
Vitreous body plus part of zonule	1,409.2	60.41	4,585.4	66.26	3.13	+5.74

Calculation 18, of the area of the anterior surface of the cornea (area of a zone of a segment of a sphere), is as follows:

$$A = \pi Dh$$

For the adult eyeball this becomes

$$A = 3.1416 \times 18.2 \times 3.4 = 194.4 \text{ mm.}^2$$

For the eyeball of the newborn this becomes

$$A = 3.1416 \times 14 \times 3 = 132.0 \text{ mm.}^2$$

Calculation 19, of the area of the anterior retinal surface, is as follows:

$$A = \pi Dh$$

For the adult eyeball this becomes

$$A = 3.1416 \times (23.6 - 1.8 - 0.22 - 0.6) \times (23.6 - 3.4 - 1.31)$$
$$A = 3.1416 \times 21.0 \times 18.89 = 1{,}246.0 \text{ mm.}^2$$

For the eyeball of newborn this becomes

$$A = 3.1416 \times (16.8 - 1.4 - 0.14 - 0.56) \times (16.8 - 3.0 - 1.05)$$
$$A = 3.1416 \times 14.7 \times 12.75 = 588.8 \text{ mm.}^2$$

SUMMARY

All these calculations, in absolute values and calculated as percentages of the eyeball, are shown in tables 2 and 3. In addition, the changes from the eyeball of the newborn to that of the adult, as multiples and as changes in percentages of the whole eye, are given. The only determinations not already described are those of the vitreous body, which was estimated as being approximately equal to the bulbar segment less all the remaining components in the bulbar portion: sclera, choroid, retina, ciliary body, intramural portion of optic nerve and lens, and also less the posterior chamber.

TABLE 3.—*Miscellaneous and Alternate Computed Values of Structures and Spaces of the Eyeball*

Structures and Spaces	Values for Newborn		Values for Adults;	Values for Adults as Multiples of Values for Newborn	Changes in Percentage Values from Birth to Maturity
	Absolute, Cu. Mm.	Percentage of Eyeball	Absolute, Cu. Mm.		
Extrabulbar portion of optic nerve..	150.2	.....	191.0	1.27	.....
Entire volume of eyeball, uncorrected	2,482.7	.....	6,892.3	2.77	.....
Combined volume of all humoral components	1,553.8	62.94	.....	3.07	+4.73
Anterior chamber.....	57.3	2.36	.....	2.60	—0.67
Posterior chamber *.....	18.5	0.76	.....	3.45	+0.16
Vitreous body *.....	1,478.1	60.83	.....	3.10	+5.25

* Including a portion of the zonule.

Palo Alto Clinic (Dr. Wilmer).

GROWTH OF THE COMPONENTS OF THE HUMAN EYEBALL

II. Comparison of the Calculated Volumes of the Eyes of the Newborn and of Adults, and Their Components

RICHARD E. SCAMMON, Ph.D.
BRANSON, MO.
AND
HARRY A. WILMER, M.D., Ph.D.*
Clinical Instructor in Medicine, Division of Neuropsychiatry, Stanford University
PALO ALTO, CALIF.

THE CALCULATED volume of the eye of the newborn and that of an adult person are shown in table 1 of a previous paper (Wilmer and Scammon 1950) and are illustrated graphically here by charts 1 through 5.

The entire eyeball increases a little less than threefold between birth and maturity. This postnatal gain is very small as compared with that of the body as a whole, which increases about twentyfold, and is even less than that of the brain, which increases about three and a half times in weight. However, the gain of the eyeball is greater than that of most of the organs of special sense; for instance, the internal ear remains almost constant in size from late fetal life to maturity, and the olfactory mucous membrane is presumed to increase 10 per cent or less in area. There is little evidence of any increase in the organ of taste as measured by the number of taste buds; in fact, the number of these structures decreases in maturity.

The ranges of postnatal increases in calculated volumes of the parts of the eye are considerable. The greatest relative postnatal gain in calculated volume is seen in the iris, ciliary body and choroid.

The adult values, measured as multiples of those for the newborn, range from 1.49, for the volume of the cornea, to 3.37, for the volume of the iris. The iris, ciliary body, choroid, vitreous body and sclera grow somewhat more, relatively, than does the eyeball as a whole. The volume of the combined coats and of all structural components increases slightly less, relatively, than does that of the total eyeball, whereas the increase of the lens, retina, anterior chamber, cornea and intrabulbar portion of

* From the Department of Neurology and Psychology, Palo Alto Clinic; formerly Fellow in Neurology and Psychiatry, Mayo Foundation, Rochester, Minn.

The art work and graphs of this paper and of the earlier paper (Wilmer and Scammon, 1950) were executed by the Mayo Art Studio.

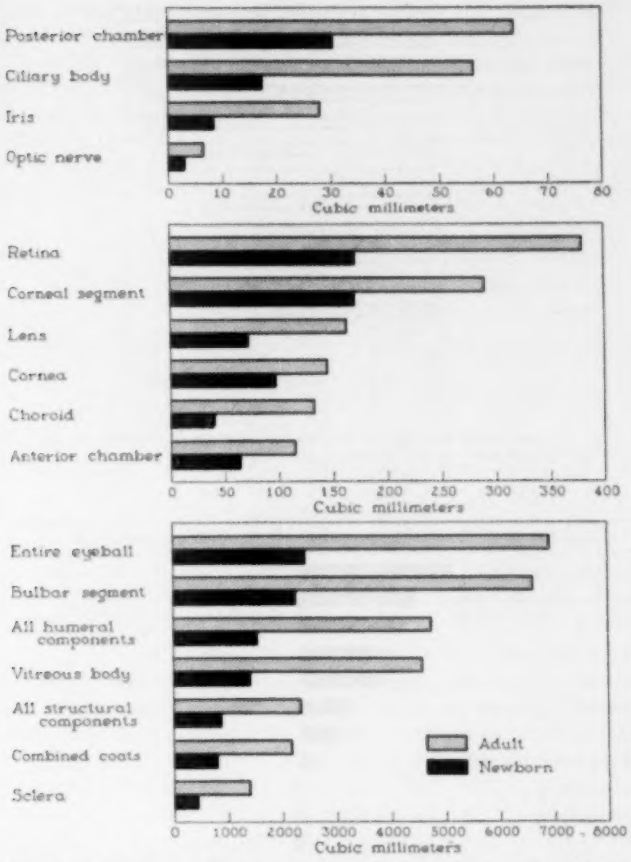

Fig. 1.—Calculated volumes, expressed in cubic millimeters, of the eyeball and its components in the newborn infant and in the adult.

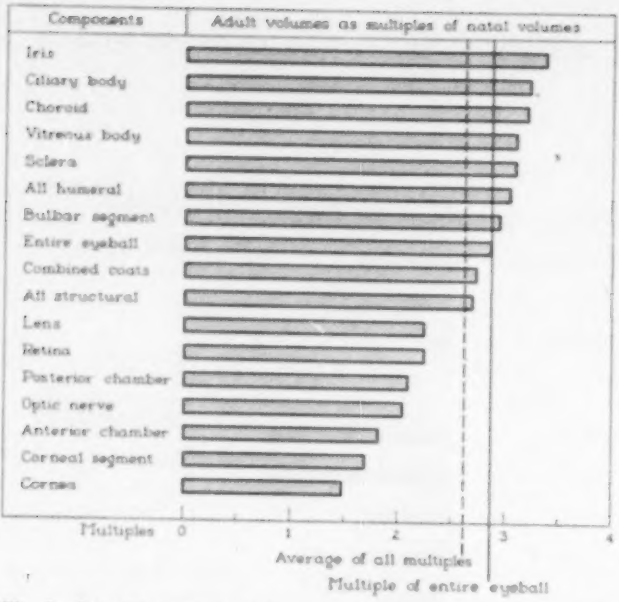

Fig. 2.—Calculated volumes of the eyeball and its components in the adult, expressed as multiples of the calculated volumes in the newborn infant.

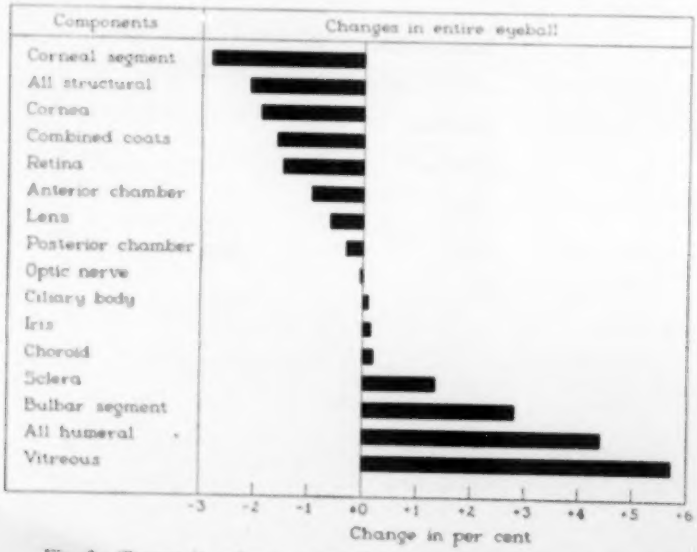

Fig. 3.—Changes in volumes, expressed as percentages of the entire eyeball volumes between birth and maturity.

the optic nerve is distinctly less. The sum of all humoral components shows a greater increase, both relative and absolute, than does the sum of all structural components.

The corneal segment of the eye shows less increase, both relative and absolute, than does the bulbar portion. This agrees with the well known observation of the relatively large cornea at birth.

These changes are shown in another manner by means of examination of the calculated figures for the percentage values of these various structures when the eyeball as a whole is regarded as unity, or 100 per cent. Speaking in general terms, the cornea, retina, lens and anterior and posterior chambers decrease in proportionate size between birth and maturity. The ciliary body, iris, choroid and intrabulbar portion of the

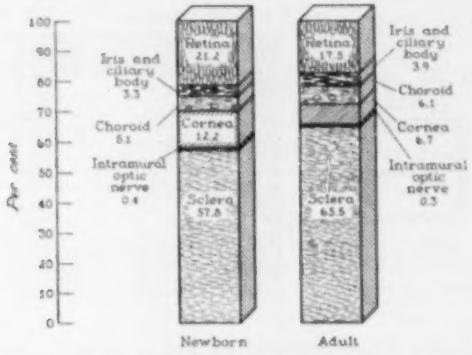

Fig. 4.—Iconometrographs illustrating the relative values (expressed as percentages of the volumes of the combined coats of the eye) of the various structures of the coat of the eye.

optic nerve maintain a fairly constant relative proportion. But the sclera, bulbar segment and vitreous body show a pronounced increase in proportionate size, ranging from a loss of nearly 3 per cent, for the corneal segment, to a gain of nearly 6 per cent, for the vitreous, during the growing period of postnatal life.

When one examines the proportional changes in the several coats of the eye in comparison with their sum, one finds that the cornea undergoes a marked decline in proportionate size from a little more than 12 per cent to a little less than 7 per cent. The retina also decreases in proportionate size, although the change is not so great. All other structures show some increase in proportionate size, this increase being greatest in the sclera (chart 4).[1]

1. See also table 1 (Wilmer and Scammon, 1950).

In general, it may be said that the volume of each portion of the eye that we have been able to measure shows a different amount of increase between birth and early maturity and that these differences are reflected in the measure of their proportionate amounts in the newborn and in the adult. However, none of these modifications appears to be as great as has previously been estimated on the basis of linear measurements. Chart 5 shows some changes in calculated areas of the eye. In this figure, *a* illustrates changes in the cornea. The anterior surface of this structure increases about one half between birth and maturity, or from approximately 132 to 194 sq. mm. The change in the area of the retina, seen in *b*, is much greater, for the internal surface of this structure is more than doubled, increasing from about 590 to nearly 1,250 sq. mm.

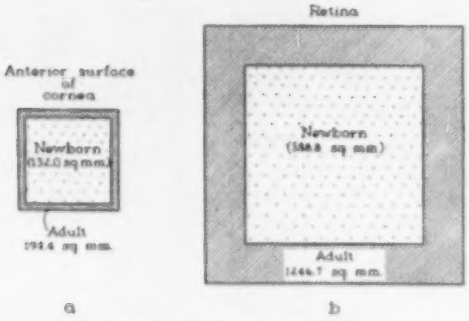

Fig. 5.—Iconometrographs illustrating the postnatal growth in calculated area of (*a*) the anterior surface of the cornea and (*b*) the internal surface of the retina.

from birth to maturity. These figures, should they prove to be correct, may require some recalculations of the number of rods and cones in the human retina.

TABLES OF COLLATED DATA ON THE DIMENSIONS OF THE EYE IN THE NEWBORN INFANT AND IN THE ADULT

The present study involves the assemblage and collation of all available published quantitative data on the dimensions of the human eyeball. The results of this procedure are summarized in tables 1 to 11. The data here presented are limited to the values for the newborn infant and, so far as possible, the values for adult persons of the third and fourth decades. However, the age range for adult persons is by no means strictly adhered to, for many observers do not give age records in connection with their figures pertaining to maturity. Values for males

TABLE 1.—*Collated Data on the Weight, Volume and Specific Gravity of the Eyeball*

Observer and Date	Sex	Number of Observations and Dimensions: Newborn No.	Newborn: Weight or Volume, Cc. or Gm.	Adult No.	Adult: Age Range, Years	Adult: Weight or Volume, Cc. or Gm.
Weight						
Krause, 1832	?	..	....	?	?	6.3-7.8
Bischoff, 1863	M	..	....	1	33	6.25
von Liebig, 1874	M	..	....	2	30-45	6.95
Weiss, 1897 *	M; F	14	2.39	5	?	7.45
Scammon and Armstrong, 1925 †	M; F	..	3.60	...	.....	.....
Todd, Beecher, Williams and Todd, 1940	M	4	2.80	104	17 and over	7.52 ± 0.05
	F	2	3.46	128	17 and over	7.39 ± 0.10
	M; F	6	3.06	232	17 and over	7.46
Collated data, adult	M; F	..	....	240	?	7.46
Volume						
Krause, 1832	?	..	....	2	?	6.6
Emmert, 1886	?	..	....	?	?	6.9
Weiss, 1897	?	..	....	5	?	7.18
Scammon and Armstrong, 1925 †	M; F	..	3.25	...	.....	.....
Specific Gravity						
Merkel, 1865, 1891 (1800)	?	..	....	?	?	1.002-1.023
Weiss, 1897 *	M; F	14	1.046	5	?	1.037

* Values for the newborn were determined from premature infants.
† Calculated by an empiric formula.

TABLE 2.—*Collated Data on the Sagittal Diameter of the Eyeball*

Observer and Date	Sex	Number of Observations and Measurements: Newborn No.	Newborn: Measurement, Mm.	Adult No.	Adult: Age Range, Years	Adult: Measurement, Mm.
Treviranus, 1828	M	..	....	2	30-40	23.1
	F	..	....	4	20-60	21.3
Krause, 1832	?	..	....	?	?	24
Krause, 1836	M; F	..	....	6	?	24.3 ± 1.54
Huschke, 1845	?	..	....	?	?	23.5
Engel, 1850 *	?	..	....	16	?	18.6 ± 0.20
Jaeger, 1861	M; F	50	17.5	..	.....	.....
Volkmann, 1869	?	..	....	?	?	24.7
Sappey, 1877	M	..	....	14	19-81	24.6 ± 0.45
	F	..	....	12	19-81	23.9 ± 0.16
Königstein, 1884	?	3	17.7	..	.....	.....
Merkel, 1885	?	..	....	?	?	24.3
Schwalbe, 1887	?	..	....	?	?	24.3
Collins, 1894 †	?	3	18.5	..	.....	.....
Schwabel, 1896	?	..	....	?	?	22.5-26
Weiss, 1897	M; F	14	16.4	5	?	23.4
Halben, 1900	?	?	18.6	..	.....	.....
Stilling, 1905	M	..	....	15	Over 20	24.3 ± 0.12
	F	..	....	?	Over 20	23.4 ± 0.73
Seefelder, 1908	?	4	17.7	..	.....	.....
Nussbaum, 1912	?	3	16.8	..	.....	.....
Scammon and Armstrong, 1925 ‡	M; F	..	17.0	..	.....	.....
Collated data, adult	M; F	..	....	140	Over 20	24.4
	M	..	....	28	Over 20	24.5
	F	..	....	12	Over 20	23.9

* Questionable data.
† Values determined on premature infants.
‡ Calculated values.

and females are given separately when sex is noted in the original records. Footnotes indicate whether the data were obtained by anatomic or by

TABLE 3.—*Collated Data on the Transverse and Vertical Diameters and the Circumferences of the Eyeball*

Observer and Date	Sex	Number of Observations and Measurements: Newborn, No.	Newborn, Measurement, Mm.	Adult, No.	Adult, Age Range, Years	Adult, Measurement, Mm.
Transverse Diameter						
Krause, 1869	?	..	....	2	?	24.0
Krause, 1896	?	..	....	6	?	24.4 ± 1.50
Huschke, 1845	?	..	....	1	?	22.5
Engel, 1850 *	?	..	....	18	?	18.0 ± 0.26
Jaeger, 1861	M; F	80	17.2	..	.....	.....
Sappey, 1877	M	..	....	14	19-79	23.4 ± 0.80
	F	..	....	12	17-79	23.5 ± 0.20
Collins, 1894 †	?	3	15.3	..	.....	.....
Weiss, 1897	M; F	14	16.4	5	?	25.3
Schneller, 1898	?	35	17.0	..	.....	.....
Stilling, 1905	M; F	..	....	15	Over 20	23.9 ± 0.16
	M; F	..	....	7	Over 20	23.5
Seefelder, 1906	?	4	18.9	..	.....	.....
Scammon and Armstrong, 1925 ‡	M; F	..	17.1	..	.....	.....
Collated data, adult, 1948	M; F	..	....	112	Over 20	23.6
	M	..	....	22	Over 20	24.2
	F	..	....	20	Over 20	23.4
Vertical Diameter						
Krause, 1869	?	..	....	2	?	23.0
Krause, 1896	M; F	..	....	7	?	23.6 ± 0.32
Huschke, 1845	?	..	....	?	?	22.0
Engel, 1850 *	?	..	....	18	?	17.4 ± 0.64
Sappey, 1877	M	..	....	14	19-79	23.5 ± 0.48
	F	..	....	12	17-79	23.8 ± 0.58
Emmert, 1886	?	..	....	?	?	25.0
Collins, 1894 †	?	3	15.3	..	.....	.....
Weiss, 1897	M; F	14	15.0	5	?	23.9
Stilling, 1905	M; F	..	....	15	Over 20	22.8 ± 0.16
	M; F	..	....	7	Over 20	23.5
Scammon and Armstrong, 1925 ‡	M; F	..	16.5	..	.....	.....
Collated data, adult, 1948	M; F	..	....	91	Over 20	23.4
	M	..	....	29	Over 20	23.6
	F	..	....	12	Over 20	23.0
Circumferences						
Merkel, 1865 (sagittal)	?	..	....	?	?	72.2
Weiss, 1897 (sagittal)	M; F	14	52.2	5	?	76.2
(transverse)	M; F	14	53.0	5	?	76.9
(vertical)	M; F	14	51.6	5	?	76.6

* Questionable data.
† Premature infants.
‡ Calculated values.

anthropometric methods from living or dead material, or by optical methods from study of the living. The specific methods employed in each of these two types of procedures have not been listed, for they

TABLE 4.—*Collated Data on the Thickness of the Coats of the Eyeball*

Observer and Date	Number of Observations and Thickness of Coats: Newborn: No.	Newborn: Posterior, Mm.	Newborn: Meridional, Mm.	Newborn: Anterior, Mm.	Adult: No.	Adult: Posterior, Mm.	Adult: Meridional, Mm.	Adult: Anterior, Mm.
Sclera (Thickness)								
Krause, 1832	..	.....	.....	.....	2	1.35	1.02	0.85
Krause, 1836	..	.....	.....	.....	9	1.35 ± 0.12	0.99 ± 0.29	0.77 ± 0.07
Engel, 1850	..	.....	.....	.....	11	.....	0.576 ± 0.183	.....
Sappey, 1877	..	.....	.....	.....	?	1.0	0.5 — 0.4	0.6
Merkel, 1885	..	.....	.....	.....	?	1.0	0.4	0.6
Schwalbe, 1887	..	.....	.....	.....	?	1.0 — 1.2	0.4 — 0.5	0.6
Merkel and Orr, 1892	16	0.918	0.469	0.515	..	.....	.....	.....
von Hippel, 1898	?	0.63	0.36	0.54	..	.....	.....	.....
Stilling, 1905	18	1.1 ± 0.09	0.8 ± 0.14	.....	68	1.2 ± 0.12	0.8 ± 0.2	.....
Thomson, 1912	..	.....	.....	.....	?	1.0	0.5	0.7
Sclera (Weight in Gm.)								
Sappey, 1877	..	.....	.....	.....	1	0.850	.....	.....
Choroid								
Krause, 1832	..	.....	.....	.....	2	0.2	0.07	0.16
Krause, 1836	..	.....	.....	.....	8	0.11 ± 0.15	.....	0.08
Engel, 1850	..	.....	.....	.....	6	0.20 ± 0.04	.....	.....
Sappey, 1877	..	.....	.....	.....	?	0.04	0.03	1.00
Merkel, 1885	..	.....	.....	.....	?	0.1	.....	0.06
Schwalbe, 1887	..	.....	.....	.....	?	0.05	0.08	.....
Merkel and Orr, 1892	14	0.09	.....	0.05	..	.....	.....	.....
Greeff, 1892	..	.....	.....	.....	?	0.1	.....	0.05
von Hippel, 1898	?	0.07	.....	0.19	..	.....	.....	.....
Venneman, 1900	..	.....	.....	.....	?	0.2 ± 0.2	.....	.....
Wolfrum, 1906	..	.....	.....	.....	?	0.30 ± 0.35	.....	.....
Salzmann, 1912	..	.....	.....	.....	?	0.22	.....	0.1 ± 0.15
Thomson, 1912	..	.....	.....	.....	?	0.1	.....	0.06
Retina								
Krause, 1832	..	.....	.....	.....	2	0.4	0.3	0.2
Engel, 1850	..	.....	.....	.....	8	.....	0.216 ± 0.053	.....
Merkel, 1885	..	.....	.....	.....	?	0.4	0.3	0.3
Schwalbe, 1887	..	.....	.....	.....	?	0.4	0.2	0.1
Merkel and Orr, 1892	14	0.095	.....	0.060	..	.....	.....	.....
von Hippel, 1898	?	0.192	.....	.....	..	.....	.....	.....
Salzmann, 1912	..	.....	.....	.....	?	0.4	.....	0.14
Thomson, 1912	..	.....	.....	.....	?	0.56	0.18	0.053

TABLE 5.—*Collated Data on the Dimensions of the Iris and Ciliary Body*

Observer and Date	Number of Observations and Dimensions: Newborn: No.	Newborn: Breadth, Mm.	Newborn: Thickness: Minimum, Mm.	Newborn: Thickness: Maximum, Mm.	Adult: No.	Adult: Breadth, Mm.	Adult: Thickness: Minimum, Mm.	Adult: Thickness: Maximum, Mm.
Iris								
Krause, 1832	..	....	....	....	2	4.86	....	0.23
Merkel, 1885	..	....	....	....	..	4.0	0.2	0.4
Schwalbe, 1887	..	....	....	....	..	4-5	0.2	0.4
Merkel and Orr, 1892	15	2.3	0.11	0.175	..	....	....	....
Quain, 1894, 1908	..	....	....	....	..	5.0	....	0.4
Tange, 1902	..	....	....	....	..	3.5-3.2	....	....
Thomson, 1912	..	....	....	....	..	....	0.2	0.75-0.3
Salzmann, 1912	..	....	....	....	..	....	....	0.6-0.4
Ciliary Body								
Sappey, 1877	..	....	....	....	..	3	....	....
Merkel, 1885	..	....	....	....	..	3.5	1.0	....
Schwalbe, 1887	..	....	....	....	..	4-5	....	....
Merkel and Orr, 1892	21	2.14	....	0.51	..	....	....	....
Quain, 1894, 1908	..	....	....	....	..	4	....	1.1
Baker, 1897	..	....	....	....	..	6-7	....	0.8
Thomson, 1912	..	....	....	....	..	2.5-4	....	....
Salzmann, 1912	..	....	....	....	..	5-6	....	....
Duke-Elder, 1932	..	....	....	....	..	4.5-6.3	....	....

would have overshadowed the text with footnotes that would hardly be clear without reference to the original sources. Practically all measurements made by optical methods were obtained from emmetropic eyes. Particular care was taken to eliminate duplicate records of data.

TABLE 6.—*Collated Data on the Diameters and Thicknesses of the Cornea*

		Number of Observations and Dimensions				
		Newborn		Adult		
Observer and Date	Sex	No.	Measurement, Mm.	No.	Age Range, Years	Measurement, Mm.
Horizontal Diameter of Base						
Helmholtz, 1867	F	*	.....	3	25-30	.....
Heuse, 1881	M; F	..	.....	70	20-60	11.6
Smith, 1882	M	..	.....	130	20-40	11.7
	F	..	.....	124	20-40	11.7
Königstein, 1884	?	?	ca. 10	..	.....	.....
Greeff, 1890	M	..	.....	?	20-60	11.3
	F	..	.....	?	20-60	11.2
Schneller, 1896	M; F	28	9.9	..	.....	.....
Seefelder, 1896	M; F	4	10.4	..	.....	.....
Grod, 1910	M	6	9.3	?	20-40	12.0
Nussbaum, 1912	M; F	3	10.0	..	.....	.....
Scammon and Armstrong, 1925 †	M; F	..	9.8	..	.....	.....
Hymes, 1929	M	11	10.0 ± 0.2	36	20-22	11.9 ± 0.04
	F	6	9.9 ± 0.1	58	20-22	11.9 ± 0.03
Vertical Diameter of Base						
Helmholtz, 1867	F	..	.....	3	25-30	.....
Schneller, 1896	M; F	28	9.2	..	.....	.....
Nussbaum, 1912	?	3	9.8	..	.....	.....
Scammon and Armstrong, 1925 †	M; F	..	9.0	..	.....	.....
Thickness (at Vertex)						
Krause, 1852	?	..	.....	?	?	1.13
Krause, 1856	?	..	.....	?	?	1.00 ± 0.07
Engel, 1860	?	..	.....	18	.....	0.8
Sappey, 1867	?	..	.....	?	?	0.8
Merkel, 1885	?	..	.....	?	?	0.9
Schwalbe, 1887	?	..	.....	?	?	0.8
Merkel and Orr, 1892	?	16	0.811	..	.....	.....
Tscherning, 1898 †	..	..	.....	?	?	1.15
von Hippel, 1898	?	3	1.15	..	.....	.....
Gullstrand, 1900 †	?	..	.....	..	.....	0.5
Thomson, 1912	..	..	.....	?	?	0.95
Thickness (at Margin)						
Krause, 1852	?	..	.....	?	?	1.25
Krause, 1856	?	..	.....	?	?	1.16 ± 0.05
Sappey, 1867	..	..	.....	?	?	1.0
Merkel, 1885	?	..	.....	?	?	1.1
Schwalbe, 1887	?	..	.....	?	?	1.1
Merkel and Orr, 1892	?	17	1.029	..	.....	1.19
Thomson, 1912	?	..	.....	?	?	1.19

* Calculated values.
† Optically determined; all others anatomically determined.

Often a measurement made by one observer is quoted by another, sometimes without citing the original source. This practice is particularly common in textbooks. All records have been screened to avoid these repetitions.

Some of the older determinations were recorded in units of measure, such as Paris inches, and in lines and grains that are now obsolete. All

TABLE 7.—*Collated Data on the Radiuses of the Cornea*

Observer and Date	Sex	Number of Observations and Dimensions: Newborn: No.	Newborn: Measurement, Mm.	Adult: No.	Adult: Age Range, Years	Adult: Measurement, Mm.
Radius of Anterior Surface						
Donders, 1864	M; F	4	6.67	319	20-40	7.80
Horstmann, 1879 *	M; F	..	....	19	17-30	7.77 ± 0.15
Wolnow, 1897 *						
Near objects	?	..	....	?	Young	6.348-7.191
Distant objects	?	..	....	?	Young	9.945-10.930
Near objects	?	..	....	?	Old	4.971-6.380
Distant objects	?	..	....	?	Old	6.009-6.001
Platenga, 1898 *	?	..	....	26	?	8.13
Tscherning, 1898 *	?	..	....	?	?	7.90
von Pflugk, 1900 *	M; F	?	?	..	.....	.....
Gullstrand, 1900 *	?	..	....	?	?	7.7
Zeeman, 1911 *	M; F	..	....	22	?	7.76
Thomson, 1912 †	?	..	....	?	?	8.4
Schiötz, 1913 *	?	..	....	470	?	7.905
Radius of Posterior Surface						
Wolnow, 1897 ‡						
Near objects	?	..	....	?	Young	4.97-6.76
Distant objects	?	..	....	?	Young	6.35-7.19
Tscherning, 1898 *	?	..	....	?	?	6.22
Thomson, 1912 *	?	..	....	?	?	6.8
Gullstrand, 1912 *	?	..	....	?	?	6.5
Schiötz, 1913 *	?	..	....	430	?	6.22

* Optically determined.
† Anatomically determined.
‡ Questionable data.

TABLE 8.—*Collated Data on the Depth of the Anterior Chamber*

Observer and Date	Sex	Number of Observations and Measurements: Newborn: No.	Newborn: Measurement, Mm.	Adult: No.	Adult: Age Range, Years	Adult: Measurement, Mm.
Adámuk and Wolnow, 1870	?	..	....	8	?	3.52
Reuss, 1877	?	..	....	6	?	2.84 ± 3.23
Horstmann, 1879	M; F	..	....	18	?	3.05 ± 0.07
Merkel, 1880	?	..	....	?	?	2.3
Stadfeldt, 1898	M	..	....	10	ca. 30	3.81
Platenga, 1898	?	..	....	26	26-50	3.036
Awerbach, 1900	?	..	....	15	?	3.4
Saunte, 1905	M	..	....	?	20-30	3.75
von Pflugk, 1900 *	?	?	2.57	..	.....	.....
Zeeman, 1911	M; F	..	....	22	?	3.6
Lindstedt, 1913, 1916	M; F	..	....	73	15-30	3.70
Raeder, 1922	M; F	..	....	60	20-40	3.46
Adler, 1924	?	..	....	?	21-50	3.42 ± 3.57
Castellana, 1924	?	..	....	?	31-50	3.56
Rosengren, 1930	M; F	..	....	50	25-30	3.51 ± 0.08
	M; F	..	....	30	30-35	3.57 ± 0.05
Imachi, 1927 †	?	..	....	?	31-50	3.31

* Anatomically determined; all other data optically determined.
† Japanese material.

these have been converted into metric measures in the accompanying tables, with the conversion factors furnished by C. and F. Noback (1865).[2]

When the individual measurements recorded by an observer were sufficiently numerous to warrant the procedure, the probable error of the mean was computed from them and is included in the present tables.

Historical Note.—The first quantitative observations on the dimensions of the eye seem to have been those made by the French ophthalmol-

TABLE 9.—*Collated Data on the Weight, Volume and Specific Gravity of the Lens*

	Number of Observations and Measurements				
	Newborn		Adult		
Observer and Date	No.	Measurement, Mg. or Cu. Mm.	No.	Age Range, Years	Measurement, Mg. or Cu. Mm.
Weight					
Smith, 1883	..	...	20	20-30	174
Collins, 1894	7	120	7	25	220
Heine, 1898	1	78.5	3	20-30	151
Smith, 1911	..	...	4	?	185
Imachi and Tadahiko, 1933, 1934 *...	?	65.6	?	20-30	172
Scammon and Hesdorffer, 1937 †....	11	65 ± 1.9	24	20-30	172.0 ± 2.0
	..	...	..	25	172.8
Volume					
Smith, 1883	..	...	20	20-30	163
Becker, 1893	..	...	?	20	155
Scammon and Hesdorffer, 1937 †....	..	...	21	20-50	162.0 ± 1.8
	..	72	..	25	166.3
Specific Gravity					
Chenevix, 1803	..	...	?	?	1,079
Davy, 1809	..	...	?	?	1,100
Nunneley, 1858	..	...	3	?	1,121
Smith, 1883	..	...	20	?	1,087
Scammon and Hesdorffer, 1937 †	..	...	20	20-30	1,060
	..	...	..	25	1,054

* Japanese material.
† Calculated values.

ogist du Petit, on the weight of the lens. They were made between 1720 and 1730. Few other quantitative observations were made in the eighteenth century. A considerable amount of quantitative data was published by Merkel (1885, 1891) Krause (1832, 1836) and Huschke (1845). They were all obtained by anatomic methods. The observations of Krause, published in 1832 and 1836, were made with great care and are particularly good. They were used later by

2. According to these factors, 127.975 Paris lines = 0.288 meter; 1.0803 grain = 0.7 Gm.

von Helmholtz (1867), and have become thoroughly incorporated in the ophthalmologic and anatomic literature, although their source is

TABLE 10.—*Collated Data on the Equatorial Diameter, Circumference and Thickness of the Lens*

Observer and Date	Number of Observations and Measurements: Newborn No.	Newborn Measurement, Mm.	Adult No.	Adult Age Range, Years	Adult Measurement, Mm.
Diameter					
Krause, 1822	..	....	?	?	6.7 -7.2
Huschke, 1845	..	....	?	?	6.76
Jaeger, 1861	70	6.35	..	.....	.....
Smith, 1883	..	....	20	20-30	8.77
Merkel and Orr, 1892	?	6.0	..	.....	.....
Collins, 1894	3	4.3	..	.....	.....
Duclos, 1895	..	....	5	20-30	9.2
Beckmann, 1896	?	6.29	..	.....	.....
Heine, 1898	1	6.25	5	20-40	9.0
Seefelder, 1908	?	6.4	5	20-30	9.2
Hess, 1910	?	7.3-7.4	2	37	9-9.5
Seefelder, 1908	?	6.4	5	20-30	9.2
Smith, 1911	..	....	4	20-40	8.68
Circumference					
Seefelder, 1908	..	....	5	20-30	29.7-30.3
Thickness					
du Petit, 1732; 1730	..	....	?	20-40	4.6
Soemmerring, 1818	..	....	?	?	4.3
Krause, 1822	..	....	2	?	4.4
Huschke, 1845	..	....	?	?	5.2
Jaeger, 1861	70	4.5	..	.....	.....
Wolnow, 1897 *					
Distant objects	..	....	?	?	3.03-3.96
Near objects	..	....	?	?	3.51-3.48
Reuss, 1877	..	....	?	?	3.89
Merkel, 1885	..	....	?	?	3.7 -4.3
Merkel and Orr, 1892	?	5.0	..	.....	.....
Collins, 1894	3	4.3	..	.....	.....
von Hippel, 1898	?	6-6.5	..	.....	.....
Heine, 1898	1	3.5	5	20-40	3.9
Stadfeldt, 1898 *	11	3.93	13	20-40	3.8
Awerbach, 1900 *	..	....	15	?	4.47
Saunte, 1905	..	....	75	20-40	3.73
von Pflugk, 1911	?	3.76	..	.....	.....
Zeeman, 1911 *	..	....	757	?	4.76
Smith, 1911	..	....	4	?	4.01

* Optically determined; all others anatomically determined.

usually forgotten. The development of the ophthalmoscope and, later, a series of other ophthalmometric instruments both increased and generally improved the quantitative data on the eye. In a number of instances, these new data have rendered the older anatomic determina-

tions obsolete. Data obtained by optical methods, when available, seem better for use in quantitative studies, not only because they frequently are more nearly precise but also because observations made on living patients eliminate the error due to postmortem changes. Moreover, material limited to a hospital population can be eliminated when optical methods are used, and the examples measured optically are, as a rule, more numerous and better selected.

TABLE 11.—*Collated Data on the Radiuses of the Surfaces of the Lens*

Observer and Date	Number of Observations and Measurements: Newborn, No.	Newborn, Measurement, Mm.	Adult, No.	Adult, Age Range, Years	Adult, Measurement, Mm.
Radius, Anterior Surface					
Helmholtz, 1867	..	..	?	?	8.8-11.9
Reuss, 1881 *	?	6	6	?	11.05
Tscherning, 1886	..	..	?	?	10.2
Awerbach, 1900	..	..	15	?	10.47
von Pflugk, 1909 *	7	5	..	..	.....
Gullstrand, 1911	..	..	?	?	11.5
Zeeman, 1911	..	..	25	?	11.05
Radius, Posterior Surface					
Helmholtz, 1867	..	..	?	?	5.88
Tscherning, 1886	..	..	?	?	6.17
Reuss, 1881	..	..	67	?	6.21
Awerbach, 1900	..	..	15	?	6.02
Saunte, 1905	..	..	75	?	5.88
von Pflugk, 1909 *	7	4.0	..	..	.....
Gullstrand, 1911	..	..	?	?	6.06
Zeeman, 1911	..	..	25	?	6.00

* Anatomically determined; all others optically determined.

SUMMARY

The eyeball increases a little less than threefold between birth and maturity. The ranges of postnatal increases in calculated volumes of the parts of the eye are considerable. The greatest relative postnatal gain in calculated volume is seen in the iris, ciliary body and choroid. The growth of the lens, retina, anterior chamber, cornea and intrabulbar portion of the optic nerve is distinctly less than that of the eyeball as a whole.

Collated data of measurements of the various components of the eyeball of the newborn and of the adult eyeball are presented in 11 tables. These data are the sources for the reference measurements and computations in our previous paper (1950).

The relative and absolute growths of the various components are illustrated in the five graphs.

Palo Alto Clinic.

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EXPERIMENTAL STUDY ON THE VITREOUS

II. Experiments on Disappearance of Red Blood Cells from the Vitreous

LUDWIG VON SALLMANN, M.D.
NEW YORK

EFFECT OF HYALURONIDASE

THE PREVIOUSLY reported experiments on isolated pig and steer vitreous [1] indicated that the decrease of viscosity due to autolytic processes enhanced diffusion of homologous hemoglobin in this substrate. No liquefying or depolymerizing effect of the enzyme hyaluronidase on hyaluronic acid—the viscous component of the vitreous jelly—could be demonstrated by the spreading rate of hemoglobin in fresh steer vitreous. However, these results could not be applied directly to conditions in the living eye of another species. In the first part of the present study the liquefying effect of hyaluronidase was examined on the vitreous of rabbit eyes in vivo. In the main experimental series the effect of the mycolytic enzyme on the disappearance of rat cells from the vitreous was investigated.

TECHNIC

Washed red blood cells served as the test substance in rabbits. A sample of the animal's own blood was withdrawn from the heart or from the marginal ear vein, and sodium citrate in isotonic concentration was added to the specimen. The cells were then centrifuged, washed three times in 0.9 per cent solution of sodium chloride and finally resuspended in a measured quantity of the saline solution to obtain a 40 per cent suspension of cells. Enzyme preparations of known activity but of varying origin, quality and concentration were mixed with suspensions of red cells in a 1:1 proportion to render a 20 per cent concentration of the cells. Throughout the procedure a sterile technic was observed; the enzyme preparations were passed through a bacterial filter before use. On several occasions tests for sterility were carried out with the cell-enzyme mixture. An amount of 0.05 cc.

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From the Department of Ophthalmology of Columbia University College of Physicians and Surgeons, and the Institute of Ophthalmology of the Presbyterian Hospital in the City of New York.

1. von Sallmann, L.: Experimental Studies on the Vitreous: I. Experiments on Diffusion in the Vitreous and on Permeability of Its Surface Condensation Layer, Arch. Ophth. **42**:583-595 (Nov.) 1949.

of it was injected with a 0.25 cc. tuberculin syringe armed with a 30 gage needle into one eye of the experimental animal, whereas the other eye received an equal amount of a 20 per cent suspension of red cells in isotonic solution of sodium chloride or in a heat-inactivated enzyme solution. At first placing of the needle was guided ophthalmoscopically to lodge the center of the hemoglobin depot axially midway between the posterior pole of the lens and the optic disk. Later the technic was standardized sufficiently so that ophthalmoscopic control was unnecessary. The pattern of distribution of the cellular material was recorded after injection, and then changes in the appearance of the cell clots and the spreading and disappearance of the cells were followed with the ophthalmoscope, first within twenty-four hours and then at two to three day intervals. The anterior segment of the eye was examined regularly with the slit lamp and the corneal microscope over periods of from three to six weeks. After this time all 64 eyes were removed and prepared for histologic examination. Twenty sections of each experimental and control eye were studied. Three batches of hyaluronidase prepared from bull testis and two samples of the enzyme prepared from rabbit testis were used. In the longer series, with heterologous material, four dilutions were employed. The homologous enzyme was made up in three dilutions. In a great number of experimental animals the intraocular tension was measured tonometrically at various intervals of the observation period.

In preliminary experiments on the liquefying action of one enzyme preparation the eyes were removed and dissected four hours after the intravitreal introduction of the enzyme. Another group of preliminary experiments dealt with the question of hemolysis of rabbit red cells by homologous hyaluronidase. The technic will be described in the text. Finally, in a third group of preliminary experiments the toxic action of bull testis enzyme on the inner structures of the eye after intravitreal injection was examined without addition of red cells.

RESULTS OF PRELIMINARY EXPERIMENTS

Liquefaction of Rabbit Vitreous by Hyaluronidase from Bull Testis.—One depolymerizing unit of the preparation used was equal to 5 micrograms of the enzyme. An amount of 500 micrograms in 0.05 cc. of fluid was injected intravitreally with a 30 gage needle in each of 4 eyes. Two control eyes were treated accordingly with heat-inactivated enzyme, and 2 eyes received the same amount of a 0.9 per cent solution of sodium chloride. After four hours all eyes were removed, and the vitreous was examined by equatorial dissection of the globe. Gross inspection revealed either complete liquefaction of the vitreous or extensive liquefaction with a small remaining portion of semisolid vitreous clinging to its base. In the controls the consistency of the vitreous was scarcely different from that observed in normal rabbit eyes.

Hemolytic Effect of Hyaluronidase of Rabbit Testis on Rabbit Red Cells.—The activity of the enzyme was comparable to that of the bull testis preparation employed in the preceding experimental series. An amount of 0.2 cc. of a 2 per cent suspension of the cells in an isotonic solution of sodium chloride was mixed with 0.2 cc. of undiluted enzyme and with serial dilutions of the enzyme, increasing in arithmetical progression. The tubes, set up in duplicate, were incubated in a water

bath at 37 C. for one hour and then transferred to room temperature of 22 C. for one hour and the results read. A second reading was made after the tubes had been left in the refrigerator overnight.

The undiluted enzyme (equivalent to 1 mg. of the preparation) had hemolyzed the red cells completely at the first reading. Slight hemolysis was noticed in the tubes with the 1:2 dilution of the enzyme; it was moderately increased at the second reading. The tubes with the remaining nine dilutions of the enzyme did not exhibit hemolysis. The results indicate, as will be seen later, that amounts of the enzyme injected into the vitreous in the experiments on absorption of erythrocytes could not have caused hemolysis of the cells.

Toxic Effect of High Concentrations of the Enzyme Preparation from Bull Testis After Intravitreal Injection.—The eyes of 6 rabbits were given intravitreal injections of 0.05 cc. of enzyme dilutions containing 125, 250 and 500 micrograms, with observance of the standard technic described. Five micrograms of the preparation was equal to 1 unit of activity. Clinically, 250 and 500 micrograms produced inflammatory changes in the anterior segment, i. e., intense flare and appearance of many cells in the aqueous humor, swelling of the iris and formation of posterior synechias. The intraocular pressure varied in an irregular manner after a transient moderate increase. Histologic examination, four weeks after injection, showed an inflammatory response in the posterior segment, which could not be recognized in vivo. There were strands of inflammatory cells in the vitreous, and infiltration of the nerve head and of parts of the retina was marked. This reaction was much less in one eye in which 125 micrograms was used and very moderate in a second eye receiving this dose.

EXPERIMENTS ON INFLUENCE OF HETEROLOGOUS HYALURONIDASE ON SPREADING AND DISAPPEARANCE OF RED CELLS IN THE RABBIT VITREOUS

Three enzyme preparations were used, their activity varying from 3 to 9 micrograms for 1 depolymerizing unit. The results are shown in table 1 and will be described individually for groups of animals which received the same amount of enzyme.

Ten Micrograms: In 4 experiments no signs of inflammation were observed, either biomicroscopically or histologically. The scattering of cellular elements around the strands or clumps of the injected cells was noticed at about the same time in the eyes treated with enzyme as in the control eyes. Formation of veils of cells, which impaired the visibility of the fundus for several weeks, and partial disappearance of this opacity also exhibited parallel courses in the two groups of eyes. Histologic examination, which was carried out four week after injection, confirmed the clinical impression that the development of various phases

in the picture was not noticeably influenced by the small amount of enzyme. The retina, optic nerve and uvea were histologically normal.

Twenty-Five Micrograms: As in the previous series, the injection of 25 micrograms of the preparation was well tolerated. The anterior segment was of normal appearance. Histologically no signs of inflammation were observed except for a small number of wandering cells on the surface of the disk in 2 of the 4 eyes which had received the enzyme mixture, but such cells were seen also in 1 of the control eyes. The scattering of red cells forty to seventy-two hours after injection and their spreading in sheets across the vitreous space in the 4 experimental eyes did not differ significantly from the findings in the 4 control eyes. Evidence of an effect of the enzyme on these phenomena was absent or questionable both in the ophthalmoscopic and in the microscopic examination.

TABLE 1.—*Effect of Hyaluronidase from Bull Testis on Spreading and Absorption of Red Blood Cells in the Rabbit Vitreous*

Dose of Injected Enzyme, Micrograms	Number of Rabbits	Increased Spreading of Red Blood Cells Over Controls	Increased Absorption of Red Blood Cells Over Controls	Inflammatory Reaction
1	2	—	—	—
10	4	—	—	—
25	4	— +	— +	—
50	5	+ +	+ +	+ — + +
125	6	+ +	+ +	+ + +
250	3	+ + +	—	+ + + +

Fifty Micrograms: The observations on this group, of 5 animals, were of considerable diversity. In 1 experiment the injection of the enzyme was followed by signs of acute inflammation in the anterior chamber. Many cells, a dense flare in the aqueous humor and intense hyperemia of the iris were observed. In this rabbit, and in a second rabbit with mild involvement of the anterior segment, signs of intense inflammation in the vitreous space were noted histologically four weeks later. A thick layer of round cells covered parts of the retina; the nerve head was swollen, and the uvea showed localized infiltration. Strands of inflammatory cells were seen in the vitreous. In these 2 globes a greater portion of the red cells had disappeared, as compared with the control eyes, which did not show inflammatory changes.

The eyes of 2 other animals of the group reacted to the injection of the enzyme less violently. The condition of the anterior chamber was well comparable to that of the control eye, and histologic examination revealed only a small number of inflammatory cells in the vitreous. In early stages the scattering of red cells around the clot was more pronounced than in the control eyes. In the latter, more blood cells

were seen histologically. This was also the case in the fifth rabbit, but the experiment had to be terminated on the fifth day because of accidental fracture of the animal's spine.

The changes in this group gave the impression of earlier spreading and disappearance of the red cells under the influence of the enzyme. But in 2 animals in which only a small part of the blood cells remained in the vitreous, there was serious inflammatory response both in the anterior segment and in the vitreous space. It cannot be excluded that the severe inflammation was caused by contamination of the enzyme, although the other animals had received aliquot portions of the same preparation.

One Hundred and Twenty-Five Micrograms: In this series two batches of the enzyme were used, one of them of a higher grade of purification. The less pure enzyme caused in 3 animals severe inflammation in the anterior segment of the same character as that described in the previous series. At the conclusion of the experiment the histologic picture showed infiltration of the nerve head and inflammatory cells in the vitreous and on the retina; this tissue was partly atrophic in one eye. The amount of packed red cells, generally lying on the retina or behind the lens, was smaller in eyes which had received the enzyme than in the control eyes. The inflammatory response in the fourth and fifth animals of this group, which had been treated with enzyme of higher purity, differed from the rest in its much milder nature. The clinical and histologic changes of inflammatory nature were here classified as slight or moderate. Phagocytosis seemed somewhat increased in eyes treated with the enzyme, but there was little difference between the experimental and the control group in the onset and degree of the spreading of the red cells and in the amount of the packed or scattered red cells which were seen histologically after the observation period of four weeks.

EXPERIMENTS ON INFLUENCE OF HOMOLOGOUS HYALURONIDASE ON SPREADING AND DISAPPEARANCE OF RED CELLS IN THE RABBIT VITREOUS

The results of intravitreal injections of hyaluronidase prepared from rabbit testis differed from the results of the previous series in several points. The injected samples of highest concentration of the enzyme had an activity of approximately 125 micrograms of the most potent bull testis preparation. The weaker solutions were of one-half or one-fourth strength. The injected doses corresponded, therefore, to amounts of 125, 62 and 31 micrograms of bull testis enzyme after the samples had been mixed with equal parts of a 40 per cent suspension of red cells. Each dilution and samples of inactivated enzyme were tested on 2 rabbits. Inactivation of the enzyme was carried out by

autoclaving at 15 pounds (6.8 Kg.) pressure. The solid coagulate was broken up by shaking before the material was injected with the red cell suspension. As usual, the fellow eyes of the 8 rabbits of this group served as controls.

The scattered effect of irritation, depending on the dose of the injected mixture, was not as distinct as that in the previous group, but very low quantities of the enzyme were not employed. Twenty-four hours after injection signs of acute iritis were observed with all three concentrations (table 2); they subsided after six to ten days. A strong flare and many cells in the aqueous and hyperemia and swelling of the iris were always seen—in 2 instances fibrinous exudate was also present, whereas the controls were free from these signs. The histologic changes in the posterior part of the eyes removed three to four weeks after

TABLE 2.—*Effect of Hyaluronidase from Rabbit Testis on Spreading and Absorption of Red Blood Cells in the Rabbit Vitreous*

Injected Enzyme	Number of Rabbits	Increased Spreading of Red Blood Cells Over Controls	Increased Absorption of Red Blood Cells Over Controls	Accompanying Inflammatory Reaction
Undiluted *	1	+	++	+
	2	+	+	+
1:2 dilution	1	++	++	+
	2	+	++	+
1:4 dilution	1	++	++	+
	2	+	++	+
Inactivated and undiluted	1	++	++	+
	2	+	++	+

* The activity of the undiluted enzyme was equivalent to that of 125 micrograms of the bull testis preparation.

the injection were much less pronounced than in experiments with bull testis hyaluronidase. A thin layer of areolar tissue on circumscribed portions of the surface of the retina was present in 2 eyes. The retina was thickened in a small area in 1 eye. In the remaining globes, the retina, optic nerve and uvea appeared histologically normal. Inflammatory cells in the vitreous forming a fine strand were noticed only once.

The spreading of cellular elements around the strands of blood cells was observed with no exception twenty-four hours after the injection of the enzyme. Veils of cells had developed twice at this early stage, extending through great portions of the vitreous. In the control eyes the spreading of cells and formation of veils did not occur before the fourth day. Clinical impressions of the end stage and histologic reports were in agreement with each other so far as the amounts of agglutinated red cells on the walls of the vitreous space were concerned. With 1 exception, the eyes given injections of the enzyme-cell mixture showed a relatively greater number of macrophages, indicating

that the otherwise moderate phagocytosis was increased. There was in 4 eyes an abundance of fine granules, which were considered breakdown products of the red cells. The eye which did not show a conspicuous increase in the phagocytic elements was the one reported as least influenced by the enzyme in the rate of disappearance of the red cells.

The inactivated enzyme produced transient swelling of the iris and a pronounced flare in the anterior chamber, similar to that in eyes which had received the active preparation, but no cells were seen in the aqueous humor. Scattering of red cells in the vitreous and development of veils were also noted early. The remaining masses of red cells in these eyes were decreased as compared with the control eyes in which suspensions of the erythrocytes in 0.9 per cent solution of sodium chloride were used. Phagocytosis was obviously more extensive in the eyes treated with inactivated enzyme.

Comment.—Verhoeff [2] twenty-seven years ago stated:

> One of the important things about the vitreous we do not know is exactly how liquefaction may come about. If we could produce liquefaction at will we would be doing an important thing in certain cases where we have vitreous opacities.

Since then not much progress has been made in solving the problem, although the clinical issue had become even more prominent with the better understanding of the part which the vitreous plays in retinal detachment. In the last fifteen years knowledge of the chemistry of the vitreous has been greatly advanced by the isolation of hyaluronic acid by Meyer and Palmer [3] and by studies of Meyer and associates [4] on the hyaluronic acid–hyaluronidase system. The identification of the spreading factor of Duran-Reynals and co-workers [5] as hyaluronidase by Chain and Duthie [6] was another important step in the development in this

2. Verhoeff, F. H., in discussion on Lister, W.: Detachment of the Vitreous, Internat. Cong. Ophth. **1**:50-69, 1922.

3. Meyer, K., and Palmer, J. W.: On Glycoproteins: II. The Polysaccharides of Vitreous Humor and of Umbilical Cord, J. Biol. Chem. **114**:689-703 (July) 1936.

4. Meyer, K.: The Chemistry and Biology of Mucopolysaccharides and Glycoproteins, in Cold Spring Harbor Symposia on Quantitative Biology, Cold Spring Harbor, L. I., New York, The Biological Laboratory, 1938, vol. 6, pp. 91-102. Hobby, G. L.; Dawson, M. H.; Meyer, K., and Chaffee, E.: The Relationship Between Spreading Factor and Hyaluronidase, J. Exper. Med. **73**:109-123 (Jan.) 1941. Meyer, K.; Chaffee, E.; Hobby, G. L., and Dawson, M. H.: Hyaluronidases of Bacterial and Animal Origin, ibid. **73**:309-326 (March) 1941.

5. Duran-Reynals, F.: Exaltation de l'activité du virus vaccinal par les extraits de certains organes, Compt. rend. Soc. de biol. **99**:6-7, 1928; The Effect of Extracts of Certain Organs from Normal and Immunized Animals on the Infecting Power of Vaccine Virus, J. Exper. Med. **50**:327-340, 1929. Hoffmann, D. C., and Duran-Reynals, F.: The Influence of Testicle Extract on the Intradermal Spread of Injected Fluids and Particles, ibid. **53**:387-398, 1931.

6. Chain, E., and Duthie, E. S.: A Mucolytic Enzyme in Testis Extracts, Letter to the Editor, Nature **144**:977-978, 1939.

field. Recent investigations of Pirie[7] on structural interaction of aggregated hyaluronic acid and the collagen-like, insoluble protein in the vitreous brought new aspects in the process of liquefaction. It was stressed in the first part of this study that the absence of a spreading action and liquefying effect of hyaluronidase in isolated steer vitreous did not exclude a specific effect of the enzyme in the living eye. It was shown in the present experimental series that injection of relatively large quantities of hyaluronidase did produce within several hours marked liquefaction of the rabbit vitreous. Such high concentrations of purified preparations exerted severe toxic side actions.[8] For this reason they could not be employed in prolonged experiments. Suspensions of the animal's own red cells were selected as indicators in studying the spreading action of smaller doses of hyaluronidase after it had been shown that such quantities of the enzyme did not hemolyze erythrocytes. It was thought that liquefaction of the vitreous jelly, as well as spreading of red cells and their disappearance from the vitreous, influenced by the use of hyaluronidase may have implication for the clinically observed absorption of blood from the vitreous. Phases of this process in the human eye and in eyes of experimental animals were studied extensively by E. Fuchs,[9] Oguchi,[10] Kiriyama [11] and others. Hemolysis of red cells and breakdown of the ghosts occur at various time intervals. Several types of macrophages are encountered; some belong to the nonpigmented ciliary epithelium, and others probably derive from the pigment epithelium of the retina. Polymorphonuclear leukocytes and histiocytes are active in phagocytosis; the latter may assume considerable size. They ingest red cells, as well as the products of their decomposition, digest them and transport them preferentially toward the posterior pole. Iron-containing and lipid particles can be demonstrated in the phagocytes, and fine granules are often seen in

7. Pirie, A.: Ox Vitreous Humor: II. Hyaluronic Acid Relationships, Brit. J. Ophth. **33**:271-283 (May) 1949.

8. Recently, MacDonald (Am. J. Ophth. **32**:96-101 [June] 1949) studied the effect of hyaluronidase on the ciliary processes after local administration in enucleated rabbit eyes, and Linn and Ozment (Some Effects of Injection of Hyaluronidase into the Anterior Chamber, read before the 18th Meeting of the Association for Research in Ophthalmology, Inc., June 1949) described tissue damage in the anterior segment of the rabbit eye after repeated injections of hyaluronidase into the anterior chamber.

9. Fuchs, E.: Zur pathologischen Anatomie der Glaskörperblutungen, Arch. f. Ophth. **99**:202-248, 1919.

10. Oguchi, C.: Ueber die Wirkung von Blutinjektionen in den Glaskörper nebst Bemerkungen über die sog. Retinitis proliferans, Arch. f. Ophth. **84**:446-520, 1913.

11. Kiriyama, G.: Experimentelle Untersuchungen über die Resorptionsmechanismen in der Glaskörperblutung und die Beforderungsmittel der Resorption derselben beim Kaninchen, Zentralbl. f. d. ges. Ophth. **42**:649, 1938-39.

the vitreous, and rarely in the anterior chamber. It was agreed on by these workers that phagocytosis and the transportation of the engulfed matter play a relatively minor part in the disappearance of blood from the vitreous. Formation of connective tissue, which occurs in intravitreal hemorrhages of the human eye, was uncommon with the technic used in the present experiments, except for the development of a strand which originated from the surface of the optic disk or from the puncture wound in the sclera.

In the present investigations, the studies with the ophthalmoscope and the slit lamp, as well as the histologic examinations, had two immediate objectives: first, to compare experimental and control eyes with regard to changes in spatial arrangement of the strands and clots of injected red blood cells, and to the spreading of these cells, veil formation and disappearance of the veils; second, to record inflammatory reactions in the anterior segment and in the vitreous space in both groups of eyes over periods of observation ranging from three to six weeks. In the series of experiments with bull testis enzymes, early spreading of red cells and development of veil-like opacities were seen when the concentration of the injected enzyme was about 50 micrograms or more. With few exceptions, it was noted that the onset of scattering of cells and the speed of absorption were linked to inflammatory reactions, which, in turn, increased with the concentration of the enzyme. Only in the group receiving 50 micrograms of the enzyme were there a few instances of increased absorption without more than a very slight inflammatory response.

It was felt that the heterologous proteins of the bull testis preparation may have exerted the strong toxic effect. Severe inflammatory response to intraocular administration of heterologous serums was repeatedly reported.[12] Therefore a potent enzyme prepared from rabbit testis was employed in our series.[13] It also caused toxic side actions, which consisted in transient iritis, but did not produce marked infiltration of the tissues of the posterior segment. With the use of this enzyme an increase in the rate of disappearance of the cells was observed in all eyes. Histologic examination suggested that the favorable course was

12. Sattler, C. H.: Untersuchungen über die Wirkung von Blutserum nach Einspritzung ins Auge, Arch. f. Augenh. **64**:390-404, 1909. zur Nedden, M. W.: Bacteriologische Blutuntersuchungen bei sympathischer Ophthalmie und anderen Formen von Iridochorioiditis, Arch. f. Ophth. **62**:193-226, 1905. Teich, M.: Experimentelle Untersuchungen über das Verhalten animalischer Gewebe im Glaskörper des Tierauges, Ber. ü. d. Versamml. d. ophth. Gesellsch. **35**:219-226, 1909. Filatov, V. P.: Ueber den Einfluss des normalen und immunhämolytischen Serums aufs Auge; abstracted, Klin. Monatsbl. f. Augenh. **46**:98-99, 1908.

13. Dr. K. Meyer prepared and purified samples of the enzyme from rabbit testis. All other hyaluronidase preparations were also extracted and purified in the laboratory of Dr. Meyer.

brought about by more intensive phagocytosis. Similar effects were observed in eyes which had been treated with heat-inactivated enzyme. This result led to the impression that a nonspecific heat-resistant factor in the preparation was responsible for both the transient inflammatory response and the speedier breakdown and transport of the cells and products of their decomposition. On the other hand, the proteinases of the phagocytes may also have reduced the viscosity of the vitreous. It is possible that the toxic side action of the preparations used overshadowed the desired specific effect of the enzyme and that the use of preparations of higher purity may modify the conclusions to which the present investigations led. It is also possible that the presence of inhibitors influenced the activity of the enzyme. It will be necessary, therefore, to repeat the studies when further progress has been made in the purification of the enzyme. Such studies should be extended again to analyze the effect of the enzyme on the intraocular pressure, which was completely irregular and inconclusive in the reported series.

SUMMARY

1. Hyaluronidase preparations liquefied in vivo rabbit vitreous within a few hours when high concentrations were used. These concentrations could not be employed in prolonged experiments because of their strong toxic side action.

2. Weak concentrations of an enzyme derived from bull testis influenced the disappearance of red cells from the vitreous to a negligible degree. Higher concentrations speeded up the disappearance of the cells but caused often severe inflammatory reactions.

3. Enzyme preparations made from rabbit testis caused also inflammatory changes, but of transient character and limited to the anterior segment. Red blood cells disappeared faster, probably owing to an increase in phagocytosis.

4. Control experiments with heat-inactivated enzymes indicated that under the experimental conditions the favorable effect was probably not connected with the specific action of the enzyme but was due to the mild irritating effect of a heat-stable constituent of the preparation.

EFFECT OF SHORT BOUTS OF ARTIFICIAL FEVER AND CHANGES IN THE BASIC METABOLIC RATE

TECHNIC

In this part of the study, albino rats were used as experimental animals. Individual samples of blood were withdrawn by heart puncture, with the animal under light ether anesthesia. With 0.5 cc. of the blood was mixed 2 cc. of a sterile solution composed of 3 Gm. of dextrose, 1.33 Gm. of sodium citrate and 0.47 Gm.

of citric acid in 100 cc. of distilled water. To avoid the use of a second general anesthesia on the same day, the mixtures were kept overnight in the refrigerator. They were then transferred to tubes which contained 7 cc. of a 0.9 per cent solution of sodium chloride and were centrifuged. Further treatment of the cell suspension was the same as that in the experiments on rabbits in the previous series. A 20 or a 10 per cent suspension of red cells was used, of which a minimal amount (about 0.01 cc.) was injected with a 30 gage needle into both eyes of the rat, under ether anesthesia. Sterile conditions were observed in the procedure. The number and heaviness of strands and clots of cells and their pattern of distribution were determined ophthalmoscopically. The findings were classified according to an arbitrary scale; i. e., extensive accumulation of blood cells was called grade 3. Here the red fundus reflex was completely obscured. In grade 2 many heavy strands were present but details of the fundus could be seen between them. Grade 1 was characterized by fine strands and scattered cells. Changes in the ophthalmoscopic picture were recorded at intervals of two to three days and tabulated. Expressed in grades, they could be plotted against time to obtain curves. The area under the curve was either calculated by integration or measured planimetrically to allow estimation of the degree of absorption over a given period. The clinical observations were supplemented by histologic examination of each globe.

In the series in which fever was induced the animals were kept in an air chamber at a constant temperature of 40 C. for thirty minutes daily for eighteen days. The body temperature was measured rectally before and after exposure to the increased temperature. Weights and tentative blood counts before and after treatment were also recorded. Fourteen rats were treated in this manner. Both eyes of 10 control rats of the same age group were given injections of their own red blood cells at the same time as the animals subjected to heat; that is, 48 eyes were followed ophthalmoscopically and examined histologically.

Changes in the basal metabolic rate were produced by thyroidectomy and by injection of thyroxin. Five litters of albino rats, consisting of 34 animals, were divided into three groups. On the first group, of 12 rats, Dr. G. Smelser performed thyroidectomy when the animals were 2 weeks old and weighed 20 to 29 Gm. The completeness of the extirpation of the gland was confirmed by retardation of growth in all instances. A second group, of 12 rats, received daily subcutaneous injections of thyroxin in a dose equivalent to 1 mg. per hundred grams of body weight. A third group, of 10 animals, was used as a control. Litter mates were distributed as regularly as possible among the three groups. A few days after initiation of the thyroxin treatment minimal amounts of a 20 per cent suspension of the animal's own red cells were injected into the vitreous of both eyes of the rats in all three series. Injections of thyroxin in the second group were continued on the basis of 1 mg. per hundred grams of body weight. The two other groups received no additional treatment. Experiments were terminated two weeks after injection of the blood cells into the vitreous, when all eyes were removed for histologic examination.

RESULTS

Exposure to a temperature of 40 C. for thirty minutes raised the body temperature of the animals 2 to 3 degrees (C.) for about one hour after the phase of induction. The heating in one session caused a loss of weight of 0.6 to 2 Gm., i. e., an average of 0.7 per cent of the body weight. Examinations of the blood which were carried out tentatively prior to and after the bouts of fever did not show significant shifts in red and white cell counts.

The amount of red cells in the vitreous of heated animals decreased in most instances at a faster rate than that in the control rats (chart 1). In several instances the absorption of the cells was considered unusually rapid. The graph does not express end results but indicates the speed of absorption within eighteen days in all stages, since the planimetric measurements of the area under the curve covered the entire period of observation. The histologic reports on the 46 eyes on the whole were in accordance with the clinical description of the end stage. Accumulation of erythrocytes on the retina, especially in the lower periphery, formation of strands and scattering of cells in the vitreous were usually recognized histologically, as they had been clinically. Microscopic examination gave further information on the nature of the scattered cells

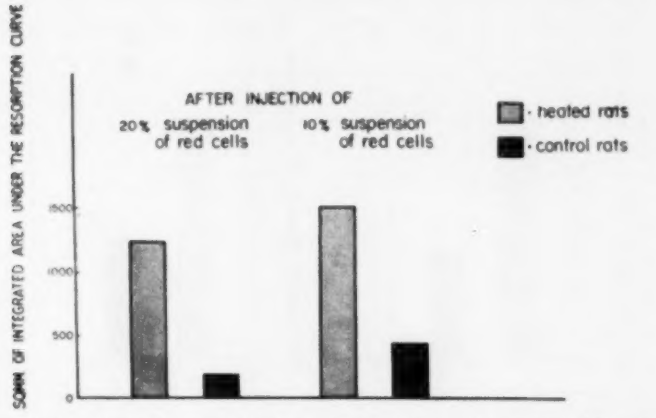


Chart 1.—Resorption of red blood cells from the vitreous of heated rats (28 eyes) and of control rats (20 eyes).

and on the presence of microphagocytes and macrophagocytes. The intensity of the phagocytosis was especially well demonstrated with the Turnbull blue stain (ferrous ferricyanide). The number of the large histiocytes with iron-containing granules showed a certain relation to the speed of absorption which had been observed with the ophthalmoscope: A low number of red cells in the 20 sections studied of each eye coincided often with the presence of many large phagocytes. It appeared that they played an important part in the early disappearance of the red cells.

In the experiments on the effect of hypothyroidism and hyperthyroidism on absorption of red cells from the vitreous, it was observed that rats treated with thyroxin developed and gained weight in a manner

similar to the controls. Thyroidectomy performed on 12 young animals resulted in retarded growth in all instances, as shown in chart 2. In table 3 the results of histologic examination, presenting the end stage, are compared with the appearance of the cellular suspension shortly after injection in the vitreous. In the thyroxin-treated group the incidence of "good" absorption (58 per cent) exceeded that in the control animals (35 per cent). The rate of disappearance was classified as low in 4 of the 24 eyes. This difference between the thyroxin-treated and the untreated group was not demonstrated when resorption was expressed in planimetric evaluation of areas under the entire absorption curve (chart 2). The discrepancy could be explained by a delay in the onset of disappearance of

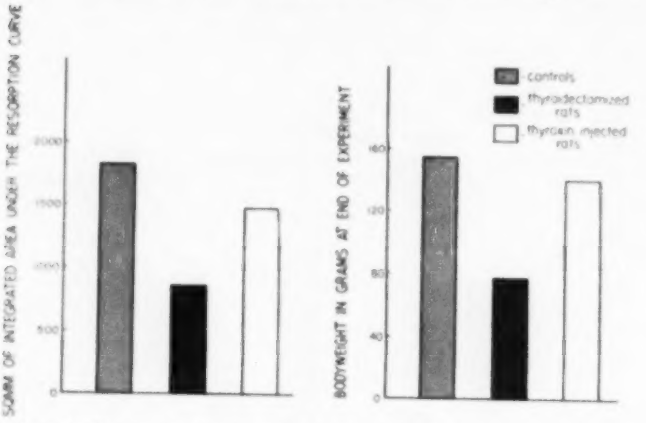


Chart 2.—Resorption of red blood cells from the vitreous and weight of rats after thyroidectomy (24 eyes) and after subcutaneous injection of thyroxin (24 eyes), and of the control rats (20 eyes).

cells in the first week or ten days after initiation of the hormone injections in 4 animals (8 eyes). This period was followed by rather rapid clearing of the vitreous in the last four to six days. Therefore the experiment suggested a trend toward increased absorption of red cells from the vitreous under the prolonged influence of thyroxin treatment.

The disappearance of the cells was slowed down in the thyroidectomized rats. This was illustrated by comparison of the initial ophthalmoscopic picture and of results of histologic examination of the eyes, as well as by planimetric presentation of absorption areas which included the clinical changes over a period of fourteen days. Here absorption was listed as poor in 46 per cent of the globes, in contrast to 10 per cent for the control group and 16 per cent for the series with injection of thyroxin. Exceptions to the general trend were encountered in all three groups.

Some of the experiments on the rate of disappearance of red cells from the vitreous were designed along lines used in the treatment of opacities in the vitreous in the human eye. The observations made with artificial fever were reported to some extent. Other approaches will be mentioned only in brief because they gave uniformly negative results. A 10 per cent solution of sodium chloride was used in the form of subconjunctival or intravenous injection in rats or rabbits. Local treatment was repeated daily for twenty-four days in 3 rats and 2 rabbits in doses of 0.1 and 0.3 cc., respectively. Daily intravenous injections (1 cc.) were continued for the same length of time in 3 rats. Hyperemia of the anterior uvea was induced in 4 rabbits by daily iontophoretic introduction of a solution of histamine dihydrochloride, 10 mg. per cubic centimeter. None of these procedures seemed to influence beneficially the absorption of red cells in the vitreous.

TABLE 3.—*Absorption of Red Blood Cells in the Vitreous of Thyroxin-Treated, Thyroidectomized and Normal Rats**

	Number of Eyes		
Absorption of Red Blood Cells	Thyroidectomized Rats	Thyroxin-Treated Rats	Controls—Normal Rats
Good	6	24	7
Medium	7	6	11
Poor	11	4	2

* Grades were obtained by comparing the initial ophthalmoscopic report with the histologic picture two weeks after injection.

Comment.—Of the technics applied, only short bouts of artificial fever repeated daily for eighteen days increased the disappearance of red blood cells from the vitreous of rats, as compared with that in control animals. There were only a few instances in which this effect of induced elevation of body temperature was not striking or questionable. Among the many biophysical or biochemical factors which may operate in artificial fever should be mentioned the increase in velocity of circulation; the change in water balance due to sweating, loss of plasma volume and restoration of the loss from fluids in the tissue spaces; leukocytosis; rise in metabolic rate, and increased enzyme activity. The loss of water in the animals during the short period of heating was indicated by the decrease in weight of about 0.7 per cent of the body weight. In tentative counts changes in the blood picture were not noticed, but the examinations were not repeated frequently enough to exclude transient shifts. It was observed that in 6 eyes a greater number of iron-containing histiocytes and of other phagocytes was encountered in the animals treated with fever than in the control animals. It is possible, therefore, that the favorable result of the heating was

brought about by more intensive phagocytic activity, in addition to any of the other factors previously mentioned.

Thyroidectomy in young rats resulted apparently in a depression of factors which govern the breakdown and disappearance of red cells in the vitreous cavity. In the series with thyroxin injections a toxic effect of the hormone, as well as the increase in metabolic rate, must be considered. Such a toxic effect of thyroxin was suggested in a study of Smelser [14] on speed of cell movement and mitotic division in the regenerating corneal epithelium of rats. Interaction of the two factors may have rendered the results ambiguous. However, moderate acceleration of the rate of disappearance was suggested in the last period of the treatment, which was limited to sixteen days. The negative results of repeated subconjunctival injections are at variance with the conclusions of Kiriyama,[11] who observed a beneficial effect of this treatment on absorption of red cells from the vitreous of rabbits.

SUMMARY

1. Short bouts of fever, produced daily for eighteen days, accelerated the disappearance of red cells from the vitreous of rats.

2. Thyroidectomy, performed on young rats, slowed the absorption of red cells from the vitreous.

3. Injection of thyroxin seemed to cause a moderately more rapid clearing of the vitreous in the latter part of the treatment period of sixteen days.

4. Subconjunctival or intravenous injections of a 10 per cent solution of sodium chloride and hyperemia of the anterior uvea induced with histamine iontophoresis were without effect.

Dr. K. Meyer provided the hyaluronidase preparations used in the experiments, and Dr. G. Smelser carried out the thyroidectomies on young rats. Miss J. Di Grandi and Miss B. Dillon assisted in various parts of the study, and Miss P. Pfaff did the histotechnical work.

14. Smelser, G.: Mitosis and Regeneration in the Corneal Epithelium of Rats as Affected by Hypo- and Hyperthyroidism, Anat. Rec. **97**:369 (March) 1948.

630 West One Hundred and Sixty-Eighth Street (32).

GENERAL ANESTHESIA IN CATARACT SURGERY

R. DOUGLAS SANDERS, M.D.
AND
NORMAN L. CUTLER, M.D.
WILMINGTON, DEL.

THIS paper constitutes a preliminary report of a new technic of administering general anesthesia for cataract extraction, with a discussion of the advantages and disadvantages.

Local anesthesia is currently used in the larger number of such operations. Although there are many instances in which general anesthesia would be preferable, the fear of unpredictable adverse results has militated against its wider acceptance.

METHODS, AGENTS AND EQUIPMENT

In 1935 Lundy [1] announced the clinical use of thiopental sodium U. S. P. (pentothal sodium®). This drug has now been used in hundreds of thousands of cases, for nearly every type of surgical procedure. Except for cataract surgery, the use of thiopental for operations on the eye has been fairly extensive. Some workers [2] have been enthusiastic because of the relative absence of difficulties of induction, the smooth maintenance and the low incidence of postoperative nausea. Others [3] have been cautious in its use because of the occurrence of sneezing, coughing, laryngospasm and respiratory depression.

Sodium evipal,® (sodium salt of C-C-cyclohexenyl-N-methyl barbituric acid), which has now been largely supplanted by thiopental sodium, was accorded the same mixed reception.[4]

From the Departments of Anesthesiology and Ophthalmology, Delaware Hospital.

Read before the Section on Ophthalmology at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1949.

1. Lundy, J. S.: Intravenous Anesthesia: Preliminary Report of Two New Thiobarbiturates, Proc. Staff Meet., Mayo Clin. **10**:536 (Aug. 31) 1935.

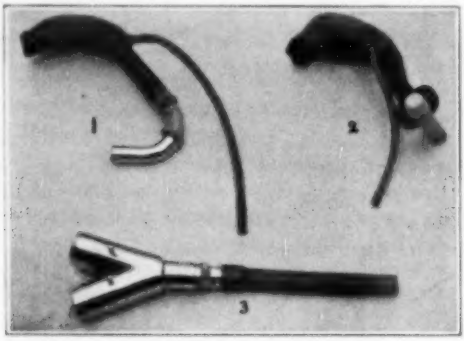
2. Reynolds, J. S.: Cataract Extraction Under Sodium Pentothal, Minnesota M. J. **29**:700 (July) 1946. Thomas, G. J., and McCaslin, M. F.: Pentothal Sodium in Ophthalmic Surgery, Arch. Ophth. **37**:542 (April) 1947.

3. Post, L., and Robertson, E. N.: Intravenous Sodium Pentothal in Ophthalmology, Am. J. Ophth. **26**:1155 (Nov.) 1943. Falls, H. F.: A Word of Caution in the Use of Pentothal in Ophthalmic Surgery, Arch. Ophth. **31** (Feb.) 1944.

4. Lyle, F. K., and Fenton, F. G.: Evipan in Ophthalmic Surgery: Further Experiences, Brit. M. J. **1**:763 (April 13) 1935. Johnstone, J. L.: Evipan Sodium in Ophthalmic Surgery, with Special Reference to Its Disadvantages, ibid. **1**:761 (April 13) 1935.

It was appreciated early that the concurrent administration of oxygen-rich mixtures of nitrous oxide by inhalation and of thiopental by intravenous injection greatly enhanced the effect of the latter, reduced the total requirement of the drug and provided better oxygenation and smoother anesthesia.

This combined method of anesthesia has been applied widely in general surgery, to the end that hundreds of workers have acquired skill in its use and familiarity with the slight respiratory changes that constitute the guiding signs of depth of effect. Insufflation of gases through nasal or oropharyngeal airways, though occasionally effective, has not been sufficiently dependable to justify its continued use. To adapt a combined inhalation and intravenous method of anesthesia to



1, 2, airways with inflatable balloons and suitable connectors; *3,* standard Y adaptor and flexible tubing for use with carbon dioxide absorber.

ocular surgery, it is necessary to provide a closed means of application of the gases which is effective, is without gross leakage, does not obtrude into the operative field and maintains a patent airway. This can be accomplished through an endotracheal tube, but coughing nearly always follows extubation, and the maintenance level of narcosis necessary for tolerance of the tube is greater than that required for a pharyngeal airway.

To meet this need, a flexible oropharyngeal airway with an inflatable balloon surrounding it was first made and used by one of us (R. D. S.). Later, to provide easier placement, a balloon similar to one described by Shipway [5] was made and applied to a standard Guedel oropharyngeal airway. In order to use this airway with a standard circle absorption anesthesia apparatus, suitable connections were devised (figure).

5. Shipway, F.: Airway for Intranasal Operations, Brit. M. J. **1**:767, 1935.

With the balloon airway in place, it is possible to obtain satisfactory confinement of the gases to the patient and apparatus, thus removing the danger of respiratory obstruction and providing a means of manual ventilation if needed.

The depth of anesthesia necessary for tolerance of an oropharyngeal airway is sufficient for the performance of ocular operations. It is obvious that if the general anesthesia is maintained at a sufficient depth, local agents sprayed in the throat are unnecessary and akinesia is adequate without block of the seventh nerve. Sneezing, tremors, ocular motion or lid squeezing, which are the result of reflexes when the patient is under light anesthesia, have therefore not been seen.

Nitrous oxide, 65 per cent; oxygen, 30 per cent, and cyclopropane, 5 per cent, compose the inhalation mixture. Addition of this small amount of cyclopropane greatly enhances the anesthetic effect of the gases, further reduces consumption of thiopental and serves to make the whole procedure much smoother. The function of thiopental in the combination is, first, induction and, later, basal narcosis. It is discontinued before the end of the operation. The amount used, therefore, is small and the recovery time shortened, with little possibility of disorientation on awakening.

Curare has been used by others [6] with thiopental, according to the methods of Baird [7] and Knight,[8] to produce akinesia and reduce laryngospasm. These factors have not been a problem in this series. Curare was used in a few cases not included in the present report, but without noticeable difference in results. Effective relaxing doses of this drug sometimes cause temporary respiratory paralysis, particularly in patients in the senile cataract age group, and its use should be attended with respectful caution.

SELECTION OF PATIENTS

Candidates for extraction of senile cataract commonly appear with a variety of physical complications, some of which may constitute contraindications to general anesthesia. Severe chronic bronchitis and emphysema, cardiac decompensation, excessive obesity and intolerance to barbiturates are the chief conditions for which local anesthesia is preferred. Intolerance to barbiturates is discovered by the administration of seconal® (monosodium 5-allyl-5-[1-methylbutyl] barbiturate) on the preoperative night.

6. Boles, W. M.: Combined Sodium "Pentothal" and Local Anesthesia for Selected Cases of Eye Surgery, with a note on the Additional Use of Curare, South. M. J. **1**:13 (Jan.) 1949. Thomas, G. J.: Personal communication to the authors, May 1949.

7. Baird, J.: Pentothal Curare Mixture, Anesthesiology **8**:75 (Jan.) 1947.

8. Knight, R. T.: Combined Use of Pentothal, Intocostrin (Curare), Nitrous Oxide, Canad. M. J. **55**:356 (Oct.) 1946.

Controlled diabetes, arteriosclerosis and hypertension without evidences of cardiac decompensation or recent arterial accident are not considered contraindications.

PREOPERATIVE PREPARATION

The patient is admitted twenty-four hours before operation. A light evening meal is given. Seconal® is given at bedtime and its effect noted. Occasionally an extremely agitated and active patient will require a second dose to secure a sound night's sleep. Clear liquids are given for breakfast and nothing by mouth after this.

A suitable dose of seconal ® is given two hours, and atropine sulfate, $\frac{1}{150}$ to $\frac{1}{100}$ grain (0.4 to 0.6 mg.), one hour, before the operation, which is done in the early afternoon.

TECHNIC OF ANESTHESIA

The anesthesia is begun by slow, intermittent injections of 2.5 per cent thiopental sodium solution through an intravenous needle in the arm opposite the side of the operation. When consciousness is lost, a face inhaler is applied and a mixture of 65 per cent nitrous oxide, 30 per cent oxygen and 5 per cent cyclopropane is administered by the carbon dioxide absorption technic. While the patient is breathing this mixture, small doses of thiopental are given until the required depth is obtained for insertion of the airway. The airway is placed in the pharynx and, after any necessary adjustments are made, the balloon is inflated and the connection is made to the tubes of the anesthesia apparatus. This establishes a relatively closed system for breathing the gases. Only after establishment of the anesthesia in this fashion is the surgical field prepared, the patient draped and the operation begun.

After the placement of the airway, small additional amounts of thiopental are occasionally needed during the course of the operation until the lens is delivered.

The depth of narcosis maintained is approximately second plane; i. e., with good activity of the intercostal muscles. The signs by which this is observed are entirely respiratory—detected by "feel" through the hand which constantly supports the chin, by hearing the respiratory sounds through the tubes and by observing the activity of the chest through the drapes and the motion of the rebreathing bag. When the anesthesia is properly performed, the maintenance period is extremely smooth.

After the operation is completed and the eye dressed, the mouth is suctioned with a catheter so that no trapped saliva may be aspirated when the airway is removed. The balloon is deflated and the airway removed without lightening of the anesthesia, to minimize the possibil-

ity of the patient's straining or gagging due to its presence. The chin is then supported by the hand until the tone of the pharyngeal muscles is regained.

EFFECT ON INTRAOCULAR TENSION

It was incidentally observed that a considerable reduction in intraocular tension resulted soon after induction with thiopental. There was no further significant change after inhalation of the gas mixture. The reduction was 35 per cent in 15 cases of cataract, 31 per cent in 6 cases of glaucoma and 35 per cent in 10 cases of normal eyes. In several of the last group, a return to the preoperative tension occurred after forty-five minutes of anesthesia.

Complications of General Anesthesia in Cataract Surgery

Total number of cases	62
Surgical complications	17
Operative	
Infection	1
Rupture of capsule	4
Loss of vitreous	6
Postoperative	
Hemorrhage into anterior chamber	6
Anesthetic complications	14
Severe induction difficulty	1
Nausea alone	3
Vomiting without strain	6
Vomiting with strain	4
Surgical complications (hemorrhage in anterior chamber) associated with anesthetic (vomiting with strain)	3

OPERATIVE PROCEDURE

It was felt that more nearly standard conditions would be met if the data were compiled from the constant technic of one operator.

Essentially the same technic was employed in all cases. No local anesthesia was used. A superior rectus suture was placed and locked on the Guyton-Park speculum. A keratome incision was made and enlarged with scissors. Two, and in some cases three, corneoscleral sutures were placed, some by the McLean procedure, some as track sutures and some in the manner recently described by Perera.[8a] Either a round pupil was formed with three peripheral iridectomies (younger age group) or a complete iridectomy (older age group) was done. An intracapsular extraction was attempted in all cases. Physostigmine was instilled after operation. The patients were got out of bed usually on the second day and were sent home in one week.

8a. Perera, C. A.: A Simple Apposition Suture for Use in Operations for Cataract, Arch. Ophth. **40**:347 (Sept.) 1948.

COMPLICATIONS

Operative.—There were 6 cases of loss of vitreous: In 2 it was due to the use of a new and unfamiliar instrument, and in 1, to a massive choroidal hemorrhage complicating retinitis pigmentosa; in 3 there was no apparent cause. In 1 case there was postoperative retinal detachment with vision limited to light perception; in 1 case the final vision was undetermined, and in 4 cases vision was normal.

Rupture of the capsule occurred in 4 cases, with resulting normal vision in 3 and a dense secondary membrane and opaque cornea in 1.

Infection occurred in 1 case; the eye has continued to be inflamed, and hemorrhage has recurred after four months. The eye will not be useful.

There was no case of prolapse of the iris.

Postoperative.—Hemorrhage into the anterior chamber occurred in 6 eyes. In 3 eyes, the hemorrhage was severe and persistent, resulting in phthisis bulbi in 2; the final status of the third eye is not definite, but a secondary membrane is present. A fourth eye has a secondary membrane and will need a discission. The remaining 2 eyes have normal vision.

Anesthetic.—Minor induction difficulties, consisting of a cough or two, occurred in 6 cases. Severe induction difficulty occurred once. The attendants were unaware that the patient had been on a spree the night before; severe salivation and coughing after induction required endotracheal intubation, and the operation was done without incident, with the patient under deep cyclopropane anesthesia. However, the immediate postoperative period was marked by coughing and vomiting. This was one of the cases in which severe hemorrhage occurred into the anterior chamber.

Accurate evaluation of postoperative nausea and vomiting is difficult, as they are not infrequently seen when local anesthesia is used. Postoperative medication, feeding and nursing undoubtedly affect the incidence. Vomiting was important only because it followed ophthalmic surgery, and it would have been considered exceedingly mild had it occurred after any other type of operative work. In the table, it is classified with and without strain.

Nausea alone occurred in 3 cases, with no ocular complications. Nausea and vomiting occurred in 10 cases, in 4 of these with strain. Of the 6 cases without strain, there were no unfavorable results and final vision was normal in 5; the sixth was the case of retinitis pigmentosa in which there occurred immediate choroidal hemorrhage, considered to be due to vascular changes rather than to anesthesia. Of the 4 cases with strain, there were no complications and vision was normal

in 1. In the other 3 cases, severe hemorrhage into the anterior chamber resulted in the loss of 2 eyes, and the final status of the third eye is not determined.

ADVANTAGES AND DISADVANTAGES OF GENERAL ANESTHESIA

Several advantages in the use of general anesthesia appear:

1. Patients who had had one eye operated on under local and one under general anesthesia expressed enthusiasm for the latter method. Preoperative apprehension is greatly lessened.

2. The difficulties of retrobulbar anesthesia, such as partial muscular paralysis and small or large retrobulbar hemorrhage, are eliminated.

3. The possibility of incomplete block of the seventh nerve and squeezing of the lids is eliminated.

4. An absolutely stationary eye on which to operate reduces the mental hazards for the operator.

5. A moderate reduction in intraocular pressure occurs.

From this preliminary survey, certain disadvantages in the use of general anesthesia are evident:

1. It takes longer to prepare the patient for operation. This takes the time of both the operator and the operating room staff.

2. The number of patients having postoperative nausea and vomiting is at present a little higher than that with local anesthesia.

3. The possibility of hemorrhage into the anterior chamber may be greater than that with local anesthesia, although in this regard the placement of the incision may be of considerably more importance than the type of anesthesia.

COMMENT

In this series the average duration of anesthesia from induction to completion of operation was forty-five minutes. The shortest period was twenty-five minutes, and the longest, one hundred and five minutes. The recovery time (until the patient responded to orders) averaged eleven minutes, with two minutes and thirty minutes as the extremes.

The amount of thiopental (pentothal®) sodium used averaged 0.64 Gm., the smallest amount being 0.45 Gm. and the largest 1.2 Gm. In no case was an analeptic needed, nor was disorientation evident after operation.

It is evident that the operative complications of loss of vitreous and rupture of the capsule are not less than the average when the extraction is done with local anesthesia, as cited by Knapp[9] from the experience

9. Knapp, A.: Present State of Intracapsular Cataract Operation, Arch. Ophth. **38**:1 (July) 1947.

of several authors. It is felt, however, that it is possible to improve on these statistics because of the factors favorable to the operator when using a general anesthetic. In no case did the administration of the anesthesia interfere with the conduct of the operation.

The postoperative complications in this small series are less than those indicated in the statistics of Hughes and Owens,[10] with the exception of severe hemorrhage in the anterior chamber. It is our present opinion that severe postoperative vomiting associated with straining may cause severe hemorrhage if the cataract incision is not placed well forward of the area of corneal vascularization.

SUMMARY

Sixty-two cases of cataract extraction with the patient under general anesthesia, using a combination of thiopental (pentothal®) sodium, nitrous oxide, oxygen and cyclopropane, are reported.

The technic of administration and the results obtained are presented, with a discussion of the apparent advantages and disadvantages.

10. Owens, W. C., and Hughes, W. F., Jr.: Intraocular Hemorrhage in Cataract Extraction, Arch. Ophth. **37**:561 (May) 1947. Hughes, W. F., Jr., and Owens, W. C.: Postoperative Complications of Cataract Extraction, ibid. **38**:577 (Nov.) 1947.

FLICKER FUSION FIELDS

III. Findings in Early Glaucoma

PAUL W. MILES, M.D.
ST. LOUIS

MANY attempts have been made in the past to alter the usual technic of taking visual fields in an effort to detect the earliest changes due to glaucoma. Some have reduced the illumination (Bair,[1] 1940; Marlow,[2] 1947; Mann and Sharpley,[3] 1947). Others (Derby, Waite and Kirk,[4] 1926; Derby, Chandler and O'Brien,[5] 1928) found that the light threshold and the dark adaptation rate are defective in early glaucoma. In all such tests perception involves visual acuity or form vision, and absolute light thresholds.

Since Phillips[6] (1933) first reported on flicker fusion frequency fields, there has been increasing interest in this entirely different type of tests. Weekers[7] (1947) has reported that flicker fusion frequency fields are depressed in cases of early glaucoma.

Unlike all other tests, determination of the flicker fusion frequency fields depends on two factors: (1) the length of the latent period between the light stimulus and the beginning of the response, and (2) the ability of cones (or groups of light-adapted elements, including cones) and their pathways to recover from the inhibitory period following one light stimulus and to become receptive to another.

From the Department of Ophthalmology and the Oscar Johnson Institute of the Washington University School of Medicine.

Read before the Section on Ophthalmology at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1949.

1. Bair, H. L.: Some Fundamental Physiological Principles in the Study of the Visual Field, Arch. Ophth. **24**:10 (July) 1940.

2. Marlow, S. B.: Fields of Vision in Chronic Glaucoma: A Comparison of Fields with Full and with Reduced Illumination, Arch. Ophth. **38**:43 (July) 1947.

3. Mann, I., and Sharpley, F. W.: Visual Fields in the Normal Dark Adapted Eye, J. Physiol. **106**:301 (July) 1947.

4. Derby, G. S.; Waite, J. H., and Kirk, E. B.: Further Studies on the Light Sense in Early Glaucoma, Arch. Ophth. **55**:575 (Dec.) 1926.

5. Derby, G. S.; Chandler, P. A., and O'Brien, M. E.: Further Studies on the Light Sense in Early Glaucoma, Arch. Ophth. **1**:692 (Dec.) 1929.

6. Phillips, G.: Perception of Flicker in Lesions of the Visual Pathways, Brain **56**:464 (Dec.) 1933.

7. Weekers, R.: L'exploration des fonctions visuelles en clinique par la mesure de la fréquence critique de fusion, Bull. Soc. franç. d'opht. **60**:331, 1947.

An injured retinal pathway may transmit correct impressions of light intensity and visual acuity because there is plenty of time for the retina to employ its powers of adaptation and analysis. But there may be changes in the reaction time and the inhibition period which could be demonstrated only by the electroretinogram. All the visual pathways are involved in flicker fusion frequency fields. Later publications will show that flicker fusion frequency fields in lesions of the chiasm, for instance, are more typical in contour and less subject to defects in acuity and cerebration than are ordinary fields.

Flicker fusion frequency fields are less affected than ordinary fields by refractive blur, peripheral aberrations, translucent defects in the ocular media, suppression amblyopia [8] and reduced intelligence or attention. Flicker fusion frequency is not greatly reduced by a small pupil, as is the light threshold, unless the miosis is of less than two hours' duration.[8] Some persons in the older age groups have normal flicker fusion frequency fields, although most show some depression, particularly peripherally.[9]

Flicker fusion frequency is a number; so gradations of perception (isopters) are measured automatically without change of target. The time required for field studies is reduced. Flicker fusion frequency, unlike tachistoscopic vision is not altered by training or fatigue.[10] The technic of taking flicker fusion frequency fields has been developed by the following workers: Phillips,[6] 1933; Niederhoff,[11] 1936; Riddell,[12] 1936; Mayer and Sherman,[13] 1938; Hylkema,[14] 1942; Weekers,[7] 1947; Miles,[15] 1949. The target light may be white, or possibly better, orange.[15] It should be 2 degrees or larger. The background should be illuminated to maintain light adaptation. Flicker fusion frequency is greatly reduced in dark adaptation and is somewhat reduced if the surround is too dark. The flicker light interval should be about 0.010 second and, if the sector

8. Miles, P. W.: Flicker Fusion Frequency in Amblyopia ex Anopsia, J. Ophth. **32**:225 (June, pt. 2) 1949.

9. Miles, P. W.: Flicker Fusion Fields: I. The Effect of Age and Pupil Size, Am. J. Ophth., to be published.

10. Tyler, D. B.: The Fatigue of Prolonged Wakefulness, Federation Proc. **6**:218 (March) 1947.

11. Niederhoff, P.: Das Flimmer-Perimeter, ein Apparat zur genauen Untersuchung des Gesichtsfeldes, Klin. Monatsbl. f. Augenh. **96**:601 (May) 1936; Untersuchungen des Gesichtsfeldes mit einem Flimmerperimeter, ibid. **107**:257 (Sept.) 1941.

12. Riddell, L. A.: The Use of the Flicker Phenomenon in the Investigation of the Field of Vision, Brit. J. Ophth. **20**:385 (July) 1936.

13. Mayer, L. L., and Sherman, I. C.: A Method of Flicker Perimetry, Am. J. Ophth. **21**:390 (April) 1938.

14. Hylkema, B. S.: Examination of Visual Fields by Determining Fusion Frequency, Acta ophth. **20**:159, 1942.

15. Miles, P. W.: Flicker Fusion Fields: II. Technique and Interpretation, Am. J. Ophth., to be published.

disk method is used, should be shorter than the dark interval. Flicker fusion frequency should be determined by judgment of the onset of flicker as the rate is decreased from a fused level, to prevent the effect of adaptation. Flicker of a constant rate may appear to stop in three minutes by adaptation.

Figure 1 shows the results for a preliminary series of patients with known glaucoma who were tested for flicker fusion frequency. The black disk indicates central flicker fusion frequency, while the white disk indicates flicker fusion frequency 10 degrees out in the temporal portion of the retina. The age of each patient is given in the line between the

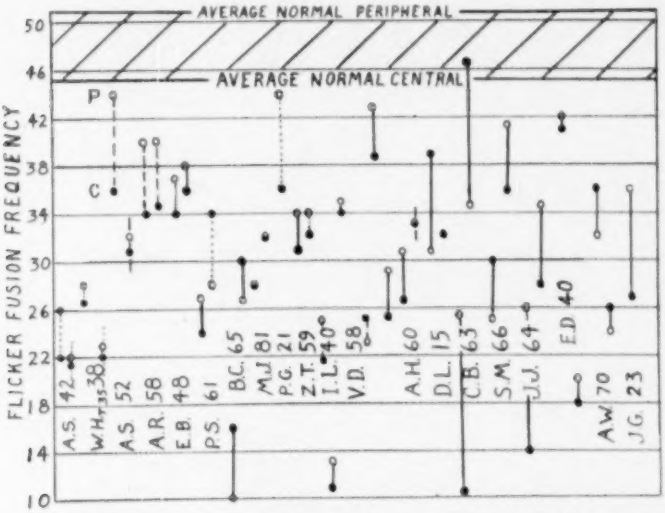


Fig. 1.—Summary of flicker fusion rates in a preliminary series of 20 patients with known glaucoma. All are well under the rates for normal eyes. The flicker fusion frequencies were taken on the central portion (closed circles) and at 10 degrees in the temporal portion of the retina (open circles) and were found to be reduced. Visual acuity and standard fields were normal. Figures after the initials indicate the age.

disks. The dotted lines indicate eyes which, although glaucomatous, had normal visual acuity and normal fields as taken by the usual methods. All fields show a reduction in flicker fusion frequency from the normal level.

Figure 2 shows normal flicker fusion frequency fields. In 1, the average central flicker fusion frequency for 10 normal subjects is shown to be 42. The annular area marked *50 +* is the extent of field in which

50 flashes per second is perceived as flicker. Part 2 shows flicker fusion frequency fields for 2 normal subjects. Although the 5 cm. circular target was 100, instead of 50, cm. from the eye, the normal flicker fusion frequency was higher because the light had been made about twice as intense —10 foot candles on a directly applied photoelectric light meter. Part *3* shows borderline normal fields. Patient S. T., aged 14, had buphthalmos

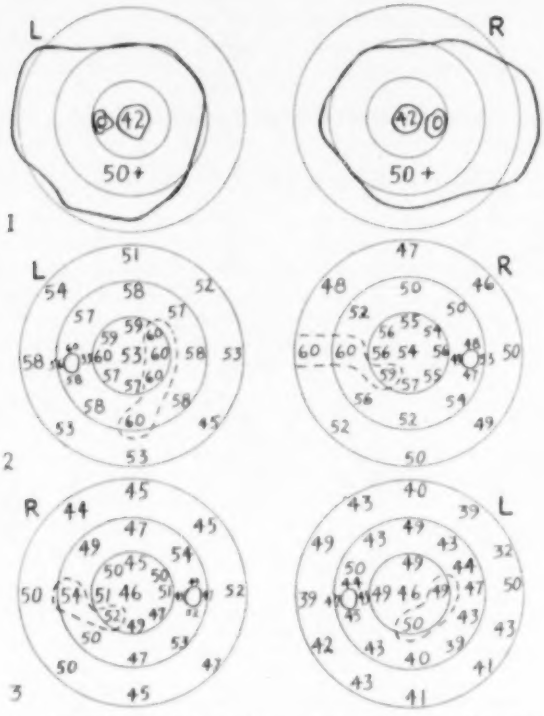


Fig. 2.—Normal flicker fusion frequency fields. *1*, average flicker fusion frequency for 10 normal subjects taken over a 60 degree field by the older perimetric technic with a 5 cm. circular target at 50 cm. from the eye; *2*, flicker fusion frequency fields for 2 normal subjects, taken on the tangent screen with the 5 cm. target at 100 cm.; *3*, borderline normal flicker fusion frequency fields for (*a*) S. T. and (*b*) M. P., taken on the tangent screen with a 5 cm. target at 100 cm.

in each eye but had apparently normal function in the eye illustrated. Visual acuity, visual fields, ocular tension and color and depth of the disk were normal. The patient had had time to adapt to the 1.5 mm. pupils, owing to the prophylactic use of pilocarpine. Patient M. P., aged 29,

had a depressive psychosis. The flicker fusion frequency field showed low areas above and below, but this was probably normal.

The highest flicker fusion frequency is not central, but inferior nasal, 10 to 20 degrees from center. The central flicker fusion frequency is normally about 5 per second lower than the peripheral. There may be a slight difference in the central flicker fusion frequency of the two eyes of a normal subject. Since suppression amblyopia * was found to show

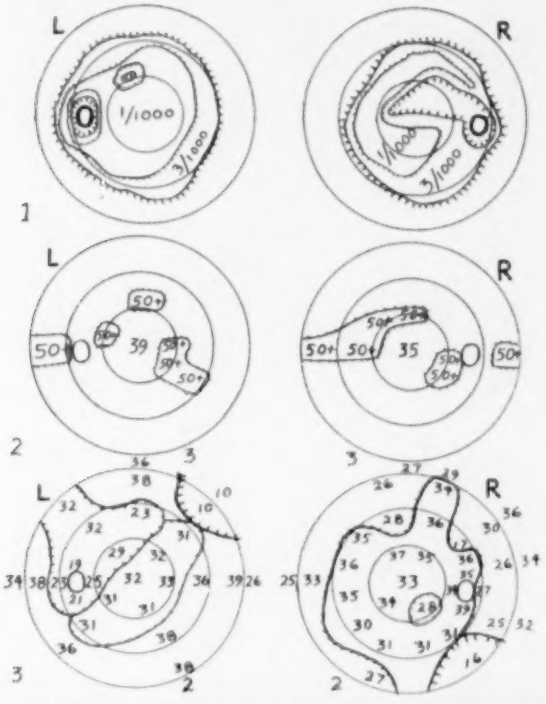


Fig. 3.—Comparison of fields taken on the ordinary 30 degree tangent screen and flicker fusion frequency fields for V. W., a Negro woman aged 37, with early glaucoma. *1*, central fields, taken Nov. 5, 1948; *2*, flicker fusion frequency fields taken on the perimeter at the same time as *1* with the 5 cm. target at 50 cm.; *3*, flicker fusion frequency fields taken on the tangent screen on Dec. 17, 1948, with the 5 cm. target at 100 cm.

an abnormally high central flicker fusion frequency, such small differences may be considered to be due to ocular dominance in many cases.

Peripheral flicker fusion frequency is normally equal in the two eyes. The rate is higher than the central flicker fusion frequency because of

diffuse synaptic relations in the retina, summation and interaction. In suppression amblyopia, the central scotoma is usually smaller than the flicker target, so that the resulting flicker fusion frequency is that of the peripheral retina. This is the only known condition in which a defective eye does not show reduced flicker fusion frequency. Central

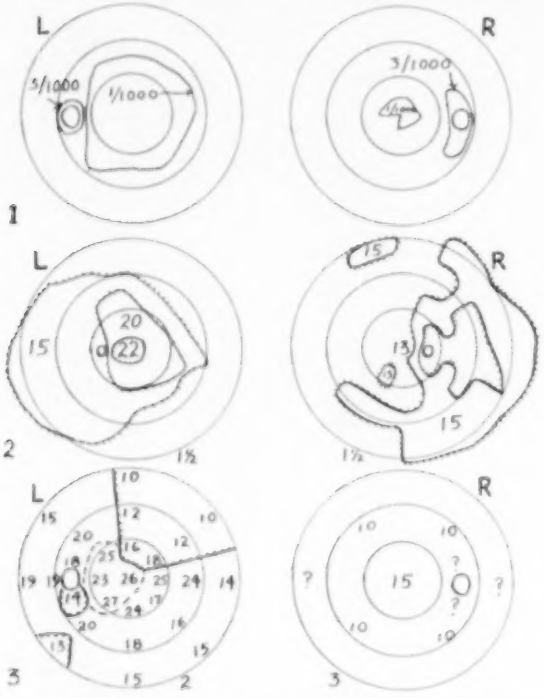


Fig. 4.—Fields for B. M., a white woman aged 66, with acute glaucoma in the right eye and suspected glaucoma in the left eye. *1*, central fields taken Sept. 13, 1948; *2*, flicker fusion frequency fields taken Sept. 13, 1948 with the 5 cm. target at 50 cm.; *3*, flicker fusion frequency fields taken March 1, 1949, four months after trephination of the right eye, taken with the 5 cm. target at 100 cm.

scotomas in cases of optic neuritis show marked loss of flicker fusion frequency, in spite of the large target. Smaller targets elicit such reduced flicker fusion frequency values in the periphery that experimental error appears, and the tests lose clinical value.

REVIEW OF CASES

Figure 3 shows the fields of a Negro woman aged 37 with chronic simple glaucoma. Visual acuity was normal, but there were cupping of both disks and typical glaucomatous progressive changes in the fields (fig. 3, *1*). Ocular tension (Schiøtz) was normal; the lability pressor test and the provocative test with a mydriatic gave negative results, and a roentgenogram showed no calcification of the carotid arteries. In figure 3, *2* shows the flicker fusion frequency fields taken

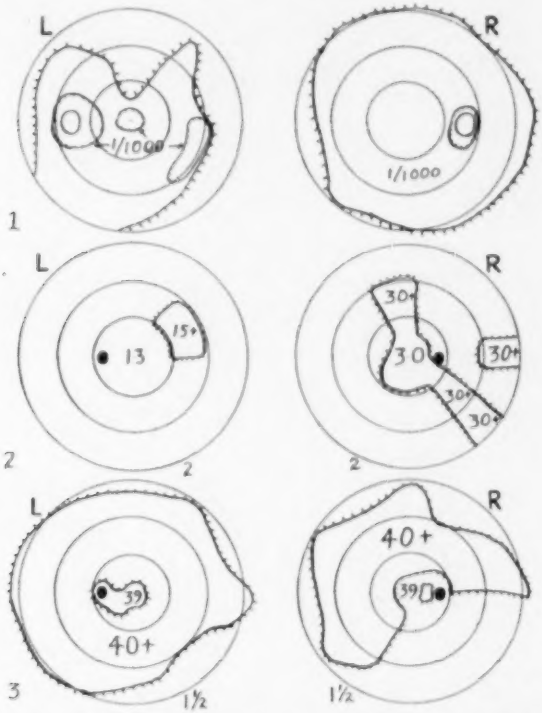


Fig. 5.—*1*, central fields for D. P., a Negro woman aged 49, with chronic narrow angle glaucoma in the left eye and suspected glaucoma in the right eye, taken Nov. 23, 1948; *2*, depressed flicker fusion frequency fields taken with a 5 cm. target at 50 cm. on Nov. 23, 1948; *3*, flicker fusion frequency fields of P. H., a white woman aged 57 with suspected glaucoma, taken with 5 cm. target at 50 cm. in September 1948.

at the same time as those in *1*. The latter reveal depression of the flicker fusion frequency, more pronounced in the central than in the peripheral portion. *3* shows fields taken on the tangent screen a month later. There are an almost total scotoma in the upper nasal quadrant of the field of the left eye and increased general depression.

Figure 4 shows the fields for B. M., a white woman aged 66, with acute congestive glaucoma in the right eye. She had had spells of pain and blurring for years, which were treated as migraine. Visual acuity was 6/12 in the right eye and 6/6 —1 in the left eye; tension (Schiøtz) was 43 mm. in the right eye and 25 mm. in the left eye. *1* shows a Seidel scotoma and a nasal notch in the central field of the right eye. The field of the left eye shows some constriction to 1/1,000 (white). Flicker fusion frequency fields (fig. 4, *2*) exhibit marked depression.

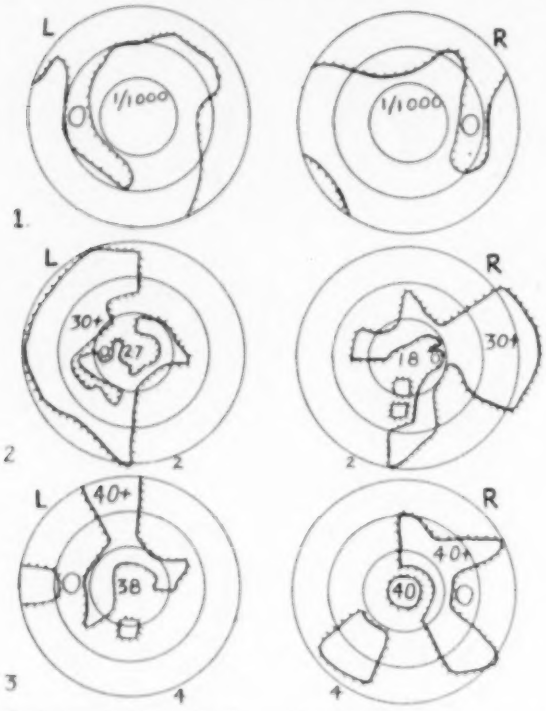


Fig. 6.—*1*, central fields of A. F., a white man aged 48 with narrow angle glaucoma, taken Sept. 23, 1948; *2*, flicker fusion frequency fields for A. F., taken with 5 cm. target at 50 cm. on September 23; *3*, flicker fusion frequency fields for G. M., a white man aged 51 with suspected glaucoma, whose ordinary (central) fields were normal, taken Nov. 21, 1948 with 5 cm. target at 50 cm.

The left field, which appeared almost normal with the ordinary technic, shows central flicker fusion frequency of 22 with peripheral values between 15 and 20. The right eye has loss of nasal field. *3* shows the flicker fusion frequency fields four months after trephining of the right eye. Unfortunately, cataract had developed, but the tension had become 13 mm. Flicker was almost imperceptible. The left eye, which had maintained normal tension all the time, when tested with

the more intense 5/100 target, showed marked depression, a Seidel scotoma and defect in the upper nasal sector. The fields as taken by ordinary technics (not shown) were unchanged.

Figure 5, *1* shows the central fields of D. P., a Negro woman aged 49, who had chronic narrow angle glaucoma. Visual acuity on June 7, 1948 was 6/6 — 1 in the right eye and 6/20 in the left eye. Tension was 20 mm. (Schiøtz) in the right

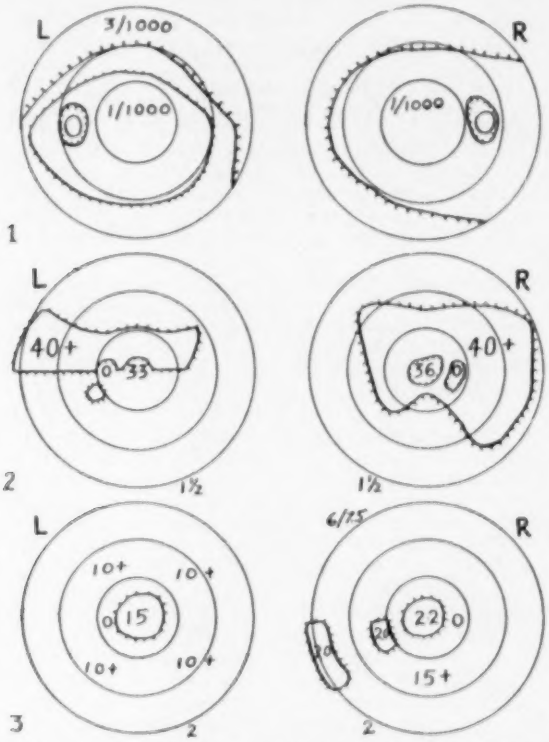


Fig. 7.—*1*, central fields for A. R., a white woman aged 59 with narrow angle glaucoma, taken Oct. 28, 1948; *2*, flicker fusion frequency fields for A. R., taken on the same date as those in *1*, with 5 cm. target at 50 cm.; *3*, flicker fusion frequency fields for S. M., a Negro woman aged 70, with chronic wide angle glaucoma and good central visual acuity, showing low flicker fusion frequency.

eye and 40 mm. in the left eye. The left disk was cupped. Gonioscopic study revealed synechias and closure of the angle of the left eye. *2* shows depression of the flicker fusion frequency field of the left eye and, more important, considerable depression of the flicker fusion frequency in the field of the right eye. In the periphery, 30 per second flicker was perceived only in patches of retina.

Figure 5, *1* illustrates flicker fusion frequency fields in a white woman aged 57, with suspected glaucoma. Her mother had had glaucoma; she had hypermetropia of 3.50 D., narrow but open angles, unusually deep physiologic cupping of each disk, tension of 17 mm. (Schiøtz) in each eye, normal peripheral and central fields and visual acuity of 6/5 in each eye. The flicker fusion frequency fields show depression and a wide sector defect in the inferior temporal area of the right eye.

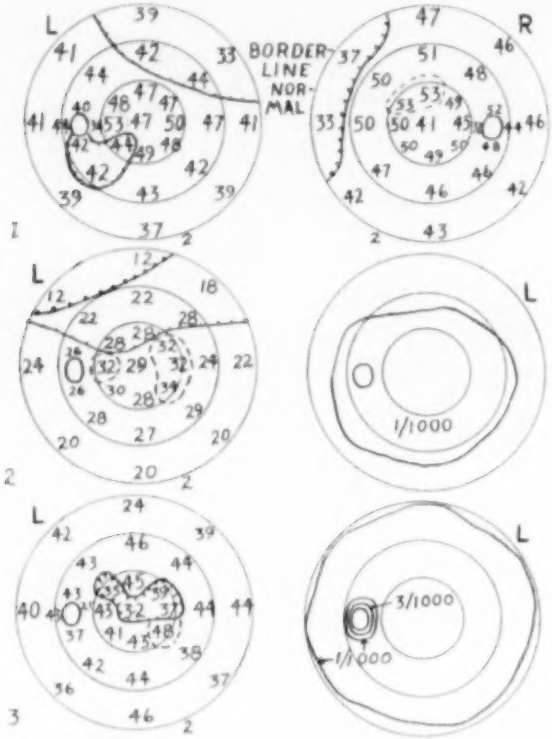


Fig. 8.—*1*, borderline normal fields for A. S., aged 54, with a painful left eye, taken Jan. 24, 1949, with a more recent tangent screen technic. A 5 cm. target at 100 cm. was used. *2*, flicker fusion frequency field and central field of the left eye of H. S., aged 50, with chronic simple glaucoma, taken Feb. 16, 1949 with 5 cm. target at 100 cm. The right eye had been enucleated for glaucoma. *3*, flicker fusion frequency field and central field for M. K., a woman aged 41, monocular, taken on Feb. 18, 1949 with 5 cm. target at 100 cm.

Figure 6 shows the fields of A. F., a white man aged 48, who had gonioscopic evidence of narrow angles, occasional peripheral anterior synechias, cupping of the disks and the scotomas shown in *1*. In *2* are presented the concurrent flicker

fusion frequency fields with central depression and patchy peripheral loss in each eye. The contours tend to fall on the vertical and horizontal meridians. Nasal depression exceeds the temporal, reversing the normal relation. *3* shows the flicker fusion frequency fields of G. M., a white woman aged 51, with suspected glaucoma. She had vague complaints of pain, increased cupping of the disk, narrow angles as seen on gonioscopic examination, dilated pupils and a change in tension in the left eye from 19 to 27 mm. (Schiøtz) in the lability pressor test. The fields were normal on three occasions. Tension varied from 23 to 25 mm. The flicker fusion frequency fields show depression, more in the left than in the right eye and more nasal than temporal.

In *1* and *2* of figure 7 are compared the central and the flicker fusion frequency fields for A. R., a white woman aged 59. The central fields are rather doubtful, but there is complete loss of the inferior field in the left eye. The diagnosis of glaucoma was based on a history of blurring spells, hypermetropia of 6.00 D., gonioscopic evidence of narrow angles and increased pressure in provocative tests. Tension on mydriasis varied from 23 to 33 mm. in the right eye and from 23 to 26 mm. (Schiøtz) in the left eye. With the lability pressor test tension ranged from 21 to 29 mm. in the right eye and from 21 to 35 mm. in the left eye. The disks appeared normal.

3 of figure 7 is included to show how low the flicker fusion frequency can drop with glaucoma in spite of fairly good central visual acuity. S. M., a Negro woman aged 70, had chronic wide angle glaucoma due to deposits of pigment. Fields taken at the same time as *3* revealed marked depression in the left eye and moderate depression in the right eye. The central field of the right eye is similar to that in *1*, for the left eye, plus a superior nasal notch. Flicker fusion frequency fields always show more depression than do ordinary fields.

Figure 8 begins a series studied by the more recent tangent screen technic. By way of review, *1* shows a borderline normal field for A. S., a Negro woman aged 54, with a painful left eye. The ordinary tangent screen fields were normal, but there were congestion and a tension of 27 mm. (Schiøtz) in the left eye, as compared with 15 mm. for the right eye. Changes in flicker fusion frequency are minimal. There are a superior nasal defect in each field and a defect below the left disk. The high point of the flicker fusion frequency is displaced from its normal inferior nasal position.

In *2* (fig. 8) are compared the central and flicker fusion frequency fields of the left eye of H. S., aged 50, who had lost the right eye from glaucoma and had chronic simple glaucoma in the left eye. The central fields was normal in February and March 1949. Visual acuity was 6/12, but probably could have been improved with glasses. Tension had never been elevated in the left eye, but he had been under treatment with pilocarpine for three years, with a tension of 22 mm. (Schiøtz). Gonioscopic examination showed a narrow angle, but there were no synechias. The flicker fusion frequency fields show great depression, centrally to 29 and peripherally as low as 12.

3 (fig. 8) shows the fields of another monocular patient, M. K., a white woman aged 41. Her right eye had been enucleated in childhood because of injury. The left eye had suffered the first attack of acute congestive glaucoma two weeks before. Tension taken at that time was 30 mm. (Schiøtz). Visual acuity was 6/5 without glasses. The ordinary fields were normal. Gonioscopic examination showed a narrow angle and no synechias. Tension was reduced to 13 mm. with 0.5 per cent pilocarpine nitrate. The flicker fusion frequency field shows definite depression, especially in the central and midsuperior areas.

In figure 9, *1* shows incomplete flicker fusion frequency fields for E. E., a white woman aged 35. The diagnosis of glaucoma was based on the history of pain and blurring and the gonioscopic view of the base of the iris touching the cornea, an observation which is admittedly questionable. Tension was 15 mm. in the right eye and 17 mm. in the left eye (Schiøtz) at the time, and the ordinary visual fields were normal. Although the central flicker fusion frequency field is normal, the

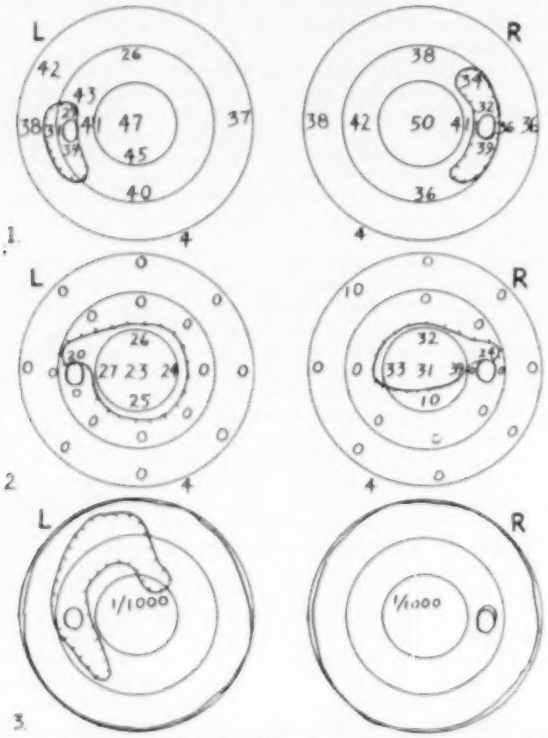


Fig. 9.—*1*, incomplete flicker fusion frequency fields for E. E., aged 35, with suspected glaucoma, taken Jan. 6, 1949 with 5 cm. target at 100 cm.; *2*, flicker fusion frequency fields for T. H., a Negro aged 69, with early glaucoma, taken on Feb. 15, 1949 with 5 cm. target at 100 cm.; *3*, central fields for T. H., taken February 2.

peripheral field is lowered generally. Frequencies in the areas above and below both blindspots are low.

2 (fig. 9) shows the greatly depressed flicker fusion frequency fields of a Negro, T. H., aged 69, as compared with the relatively normal central fields in *3*. Evidences of glaucoma included the Seidel scotoma (*3*), deep cupping of the disks and

stabilization of tension with pilocarpine at 23 mm. in the right eye and 23 mm. in the left eye (Schiøtz).

Figure 10, *1* shows the flicker fusion frequency fields of M. D., a Negro woman aged 59, who had early glaucoma but normal visual acuity and ordinary tangent screen fields. A tension level of 28 mm. (Schiøtz) for each eye was reduced to 12 and 22 mm. respectively with pilocarpine. The flicker fusion frequency fields show general depression in both eyes, especially the left eye, in which the flicker

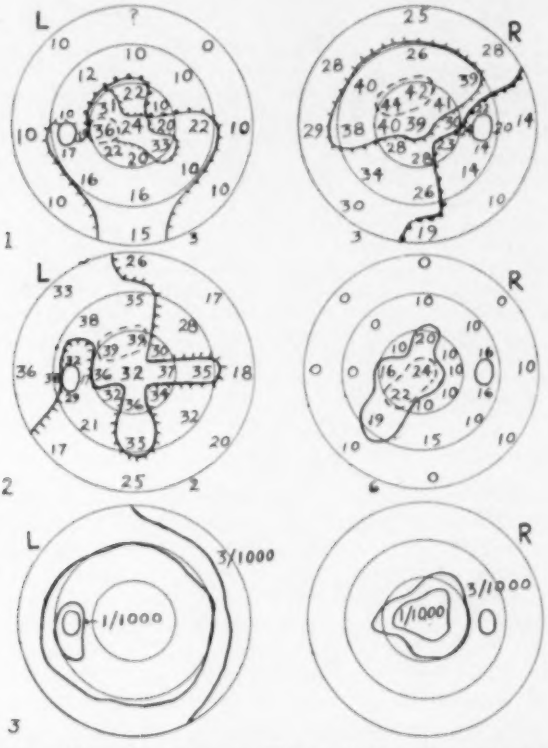


Fig. 10.—*1*, flicker fusion frequency fields for M. D., a Negro woman aged 59, with early glaucoma and normal visual acuity and normal ordinary fields; *2*, flicker fusion frequency fields for P. S., aged 58, with early glaucoma in the left eye and more advanced glaucoma in the right eye, taken Feb. 18, 1949, with 5 cm. target at 100 cm.; *3*, central fields for P. S., taken Feb. 18, 1949.

fusion frequency nearly disappears in the periphery and the upper nasal quadrant. The high point of the flicker fusion frequency is displaced temporally, and the blindspot is continuous with the scotomatous periphery superiorly. The right field shows inferior and temporal defects and baring of the blindspot. The high point of the flicker fusion frequency is displaced superiorly.

In *2* and *3* (fig. 10) the flicker fusion frequency fields are compared with the central fields of P. S., aged 58, who had been treated for glaucoma by trephination of the right eye in 1944. The present visual acuity was 6/15-1 in the right eye and 6/6-3 in the left eye. Tension was 16 mm. in the right eye and 21 mm. in the left eye (Schiøtz). The central field of the left eye (*3*) suggests suggestive glaucomatous change, while the flicker fusion frequency field (*2*) shows marked

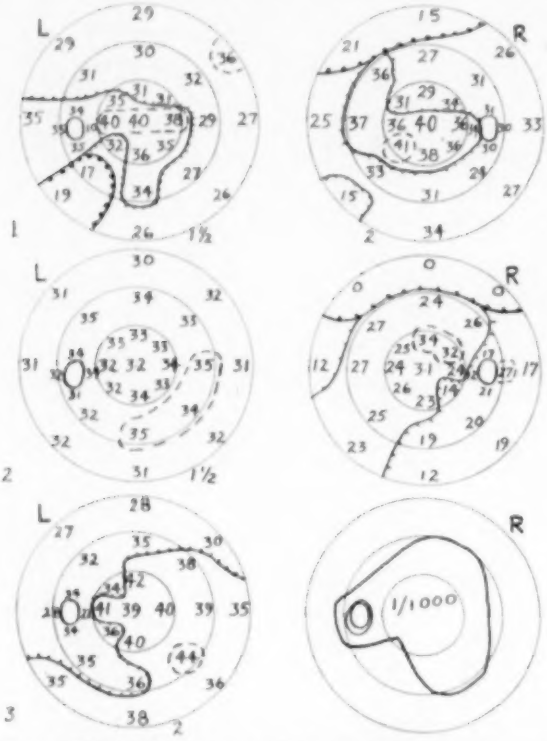


Fig. 11.—*1*, flicker fusion frequency field for H. F., a Negro woman aged 36, with chronic simple glaucoma in the left eye and an ordinary field, taken March 1, 1949, with 5 cm. target at 100 cm.; *2*, flicker fusion frequency fields for M. W., a Negro aged 73, with narrow angle glaucoma, who could not understand the usual tests, taken with 5 cm. target at 100 cm. on March 1, 1949; *3*, flicker fusion frequency field and central field for the left eye of G. H., aged 65, with glaucoma and aphakia, taken with 5 cm. target at 100 cm. on Jan. 21, 1949.

depression and baring of the blindspot. The peak flicker fusion frequency is displaced to the superior temporal field, and there is more nasal than temporal loss of flicker fusion.

Figure 11, *1* shows the flicker fusion frequency fields of H. F., a Negro woman aged 36, who has had considerable medical attention for years. In April 1947 chronic simple glaucoma was discovered; tension at the time was 25 mm. in the right eye and 15 mm. in the left eye (Schiøtz). The fields were normal, but a gonioscopic view of several peripheral anterior synechias and deposits of pigment in the angles suggested glaucoma. In December 1947 the lability pressor test changed the tension in the right eye from 17 to 29 mm. and in the left eye from 19 to 25 mm. The flicker fusion frequency fields show little central depression, but pronounced general peripheral loss. There is suggestion of a homonymous defect in each left inferior field. There is more nasal than temporal loss.

2 (fig. 11) shows flicker fusion frequency fields for M. W., a Negro aged 73, who had narrow angle glaucoma in each eye. The lability pressor tests raised the tension from 23 to 28 mm. in the right eye and from 24 to 30 mm. in the left eye (Schiøtz). This case is interesting because ordinary field technics availed nothing. The old man could not outline the physiologic blindspots and could not understand the test. Flicker fusion frequency tests seemed reliable and satisfactory. *2* shows general depression in the left eye and an inferior temporal notch and scotoma in the right eye.

In *3* are compared the flicker fusion frequency field and the central field of the left eye of G. H., aged 65. Visual acuity was normal in spite of aphakia and glaucoma. The right eye, not illustrated, had advanced glaucoma; the flicker fusion frequency field was 28 centrally and 10 peripherally. The flicker fusion frequency field of the left eye shows central and peripheral depression and a large temporal scotoma, including the blindspot and an arcuate area on each end.

Another patient, H. M., a Negro aged 60, was tested in March 1949. He had early glaucoma with normal visual acuity and fields. The flicker fusion frequency field of his left eye resembled that of the right eye in *1* and the field of the left eye resembled that of the right eye in *2* of figure 10.

COMMENT

These preliminary case studies do not represent the ultimate in the representation of field defects associated with glaucoma by flicker fusion frequency determinations. The technic and results will certainly be improved. However, at present, it is certain that when changes in field occur the changes in the flicker fusion frequency fields are greater. When the field contours did not correspond exactly, additional areas should have been tested for flicker fusion frequency.

Many diseases other than glaucoma, including the sclerosis and degeneration of old age, lower the flicker fusion frequency out of all proportion to visual acuity and ordinary field changes. It is probably too soon to say just what changes in flicker fusion frequency fields are peculiar to glaucoma. In this series of cases the flicker fusion frequency fields all showed depression, but not so uniformly as is common in controls among persons in the older age groups.[16] In the fields of glaucomatous eyes there were commonly (20 of 33) more nasal than temporal depression and more peripheral than central loss. The normal

16. Miles, footnotes 9 and 15.

high area in the inferior nasal region was lost in 16 fields. The Seidel scotoma, or baring of the blindspot, occurred in 25 of 32 eyes.

The second method of taking flicker fusion frequency fields, in which the flicker fusion frequency is determined separately in about 28 different areas, is considered more exact. The use of a 30 degree, 1 meter perimeter, instead of the tangent screen, would be a desirable improvement.

SUMMARY AND CONCLUSIONS

Twenty-four eyes with normal visual acuity and fields in which the diagnosis of early glaucoma was reasonably well established showed defective flicker fusion frequencies.

Apparently, in diseases affecting visual perception the latent period following a stimulus and the duration after the stimulus and response of the inhibitory period combine to reduce the flicker fusion frequency before acuity and form vision, and possibly light thresholds, are affected.

Flicker fusion frequency is a phenomenon well suited to tests of perception in the diagnosis of diseases of the retina and optic tracts.

Washington University School of Medicine.

Various members of the house staff and visiting physicians in the Department of Ophthalmology, Washington University School of Medicine, did the work-up on some of the patients.

ABSTRACT OF DISCUSSION

DR. LAWRENCE T. POST, St. Louis: In considering any new diagnostic procedure for determining the presence, progress or severity of glaucoma, the following questions are pertinent: 1. What, if any, new knowledge about glaucoma has been established through this procedure? 2. Is this method more sensitive than other methods? 3. How does it compare in speed with other tests? 4. Might it replace any test or be complementary to any test? 5. Is it repeatable? 6. Is the equipment readily available to all ophthalmologists, especially with respect to space required and expense? 7. Is its interpretation sufficiently simple to be understood by readers of the literature? 8. Can it be recorded accurately?

In studying Dr. Miles's work, the following answers to these hypothetic questions seem justified.

1. The use of flicker fusion frequency tests in the study of glaucoma has so far produced no new information about the site or the cause of injury to the receptor or nerve. Neither has it promised to give any pathognomonic sign of glaucoma. Dr. Miles believes, however, that if the eye has normal flicker fusion frequency fields there is no glaucoma, and that no other method of taking fields will show any defect whatever.

2. The test is much more likely to show defect in eyes with minimal disease or degeneration than ordinary field tests, though field studies with reduced illumination and varied targets might with great expenditure of time give as much information.

3. Gradations of density are obtained automatically with flicker fusion frequency fields without repeating the test with various targets. The time required is much reduced.

4. Until more definite field characteristics peculiar to glaucoma can be shown, flicker fusion frequency fields do not replace other technics. On the other hand, Dr. Miles reports that in the diseases of the optic nerve and tracts the flicker fusion frequency fields are unquestionably superior to the ordinary tests.

5. In normal eyes under laboratory conditions flicker fusion frequency findings have been shown by several different investigators to be repeatable within a range of from 1 to 3 per cent on consecutive days, but the fields are simpler to take by this method than by the normal methods when one is dealing with unintelligent patients.

6. The equipment is practical for general use. The target is on the end of a wand and is handled just as any perimeter target. About the same space is required as that for ordinary perimetry.

7. Recording is simple and accurate. Interpretations may change as the method is given further trial, and I believe that further studies are well worth continuing.

Dr. Paul W. Miles, St. Louis: I merely want to express my appreciation for the help Dr. Post has given me in this work and to thank him for his discussion.

USE OF CURARE IN CATARACT SURGERY

DANIEL B. KIRBY, M.D.
NEW YORK

THE CATARACT surgeon is enabled to perform his task with greater delicacy and precision when the patient and his eyes are quiet and relaxed. Rigidity and muscular spasm may be the effect of apprehension, fear or worry, or they may be reflex to pain or discomfort. They are the source of many of the complications arising during the operation.

PROBLEM OF MUSCULAR RIGIDITY AND SPASM

The manner in which muscular rigidity and spasm may affect the patient undergoing cataract surgery is manifold.

The Ocular Muscles.—The orbicularis, corrugator and superciliaris muscles have long been indicated as the "squeezing muscles," and the patient reacting by contracting these muscles, is known as a "squeezer." Bell's phenomenon of the upward rolling of the eyes when one or both are closed is familiar. The inadvertent casting about of the eyes, their aimless or incoordinate rolling, or, after an attempt to look down on command, their drifting upward may all be annoying and disconcerting to the surgeon. The extrinsic ocular, or orbital, muscles are usually well balanced in their contractions and in the relaxation of their antagonists, so that perfect coordination in the associated movements is produced. Under stress of emotional disturbance they may all seem to contract at once, increasing intraorbital and intraocular pressure. The movements are then not controlled or directed by visual percepts. The incoordination produced by abnormal nerve stimuli accounts for the movements of the globes.

The Muscles in General.—The surgeon who is interested in the whole patient rather than in the eyes alone will observe the rigidity of the muscles of the jaw and neck and the skeletal muscles. He will note the changes in respiration. The patient may breathe very rapidly, or he may, as he usually does, hold his breath. He has all the phenomena of stage fright, "freezing," because he cannot overcome his fear neurosis and his inability to cooperate.

Read before the Section on Ophthalmology at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 10, 1949.

EFFORTS TO OVERCOME MUSCULAR RIGIDITY AND SPASM IN CATARACT SURGERY

In the era which preceded the advent of adequate anesthesia, the surgeon sought to allay pain and overcome rigidity with soporific sponges or potions. Operations were necessarily performed quickly, so that, if possible, they were over before the patient had a chance to contract his muscles. The fairly recent use of cocaine and synthetic substances for local anesthesia, by instillation and injection; of sedatives which allay apprehension and depress the centers concerned with consciousness; of effective general analgesic agents, and, finally, of general anesthetic drugs has helped much to allay or overcome general muscular rigidity and spasm. Efforts have also been directed toward elimination of spasm of the palpebral muscle. Palpebral akinesia, produced by the methods of Van Lint [1] and O'Brien,[2] has been a great boon. Benedict stated that in the case of bad "squeezers" both sides may be blocked. Orbital akinesia produced by injection into the orbital muscle cone or by retrobulbar injection has effected deep local anesthesia and akinesia of the rectus muscles in many cases. The superior oblique is not affected by this injection, as it is well outside the muscle cone. The inferior oblique may be affected if the injection is directed at its median portion. The frequency of embarrassing proptosis caused by retrobulbar bleeding may be said to be a contraindication to the routine use of retrobulbar injection. Although it is admitted that the procedure has been used often with great satisfaction, I have given up retrobulbar injection in favor of anterior subconjunctival injection and injection under Tenon's capsule for local anesthesia. If the patient is not hypersensitive to tetracaine hydrochloride, I combine this drug, in 0.5 per cent solution, and potassium sulfate, 0.4 per cent, with the procaine for deep, long-lasting effect. The epinephrine which is used to localize and prolong the action of the procaine has not produced vasospasm often enough to be contraindicated. It may, however, add to the nervous apprehension of the patient.

The superior rectus or bridle suture has not been attractive to me, for I do not care to have the eye forcibly looking down, or to have it tied down, for the purpose. Untoward upward movements of the globe by contraction of the powerful inferior oblique muscle or of other muscles may cause disastrous pressure on the globe. I have found it necessary to search for other means of controlling rigidity and spasm of the orbital and general muscles.

The Measures Used.—It may be repeated that every effort is made to produce relaxation and confidence in the patient. He is not made a

1. Van Lint, A.: Temporary Paralysis of the Lids in Cataract Surgery, Ann. d'Ocul. **151**:420, 1914.

2. O'Brien, C. S.: Akinesis During Cataract Extraction, Arch. Ophth. **1**:447 (April) 1929.

partner in the operation, is not trained to look down, is not asked to cooperate, or to take part in the procedure and does not expect to be blamed for the complications. He is asked only to be there and to relax. Of course, he must have sedation. The barbiturates are the most useful; of these, phenobarbital is preferred for its long-lasting action, and pentobarbital sodium for its deep and rapid effect. These drugs are given, according to the tolerance and needs of the patient, on the day and the night before and on the morning of the operation. Chloral hydrate is very useful for some patients. For basal analgesia, meperidine (demerol®) hydrochloride, 50 mg., may be given intramuscularly one hour before the operation to afford time for tissue analgesia as well as for the added sedative effect. At the time of the operation, phenobarbital sodium (sodium luminal®), pentobarbital sodium or more meperidine hydrochloride may be given intravenously. Up to 100 mg. of meperidine hydrochloride should not produce ill effects. The use of sedatives and analgesics is governed by the reactions of the patient, his nervous apprehension and hyperalgesia. Palpebral akinesia and deep local anesthesia are always employed. They may be useful even with intravenous use of thiopental (pentothal®).

Persistence of Muscular Spasm and Rigidity; Hyperkinesia.—The deep physiologic reflex of muscular rigidity and spasm may persist after all the measures mentioned. It is one of the primordial defense mechanisms and is not overcome even by loss of consciousness in the early stages of general anesthesia. Even in the somnolence or sleep induced by sedatives, the patient who does not have adequate basal analgesia, palpebral akinesia and local anesthesia may react violently with muscular spasms to the discomfort or pain of surgical manipulation. The surgeon fears the excessive use of sedatives or of narcotic and general anesthetic agents because of the possibility of trauma to the organism and of the nausea and vomiting which may be produced. The frequency of unfavorable reactions after some forms of general anesthesia has been an expression of the anoxia produced by the anesthesia and its depth. The search for an agent which would overcome muscular spasm and rigidity after consciousness has been abolished in general anesthesia, and which would permit lightening of the anesthesia has led to the application of the long-known, but only recently refined, muscle-paralysant drug curare. Its use has been well received by general surgeons because it permits of greater ease of operating, with the patient relaxed and quiet and under reduced or light, nontoxic anesthesia.

USE OF CURARE

General Considerations.—The South American arrow poison curare has been purified and standardized for reliable clinical use. It has desirable muscle-relaxing properties. It has been used as an adjuvant to general anesthesia, in the shock therapy of psychopathic patients, in

carrying out certain skeletal manipulations and in the therapy of certain spastic neurologic disorders. It is contraindicated or to be used with caution in cases of myasthenia gravis. It may be used for diagnostic purposes in cases of early myasthenia gravis, as, for example, when only ptosis is present. Neostigmine is an antidote to its effect, which is on the myoneural junction. It acts by depressing or blocking the transmission of nerve impulses at the nerve ending in voluntary muscle by inhibiting the response to acetylcholine.

Two of the refined preparations of curare are intocostrin[3] (purified Chondodendron tomentosum extract) and, more recently, the crystalline salt, *d*-tubocurarine chloride. Both are water soluble. Standardization for uniformity and quantitative effect is made by the head drop cross-over method in rabbits, 1 curare unit now being defined as the activity of 0.15 mg. of pure recrystallized *d*-tubocurarine chloride pentahydrate. The number of units in the products of various manufacturers varies; 3 mg. is equivalent to 20 units.

Order of Development of Depression of Voluntary Muscles.—It was the sequence of the development of depression of voluntary muscles which first attracted me to the clinical trial and use of curare. It was reported that the initial haziness of vision, ptosis, imbalance of the extrinsic ocular muscles and inability to raise the head were followed by relaxation to complete paralysis of the long muscles of the back and of the extremities. The order followed is similar to that of the development of myasthenia gravis. Larger doses of curare affected the intercostal muscles and the diaphragm. No mention has been made of individual hypersensitivity, except to impurities in the preparations. Apparently, the effect of the drug is quantitative. Recovery from a single dose proceeds in the inverse order, taking fifteen to twenty minutes. The ocular muscles are the first to be affected and the last to recover. These properties seemed ideal for production of orbital and general akinesia with local anesthesia as an adjuvant to general sedation and analgesia for cataract surgery without exceeding the safe limits of dosage of any of the drugs used. The unfavorable effect of the low doses of different-acting sedatives, analgesics and curare as used is apparently not cumulative.

Reports on the Clinical Use of Curare; Priority in Its Use for Cataract Surgery with Local Anesthesia.—Griffith and Johnson (1942)[3] were the first to use curare as an aid to anesthesia. Cullen[4]; Brody[5];

3. Griffith, H. R., and Johnson, E.: The Use of Curare in General Anesthesia, Anesthesiology **2**:418, 1942.

4. Cullen, S. C.: Clinical and Laboratory Observations on the Use of Curare During Inhalation Anesthesia, Anesthesiology **5**:166, 1942.

5. Brody, J.: The Use of Curare in Sodium Pentothal-Nitrous Oxide-Oxygen Anesthesia, Anesthesiology **6**:381, 1945.

Cole [6]; Whitacre and Fisher [7]; Adams [8]; Gross and Cullen [9]; Fegler [10]; Schmidt [11]; Macon and Bageant [12]; Baird, Johnson and Van Bergen [13]; Harroun, Beckert and Hathaway [14]; Shane [15]; Berger, and others have contributed significant reports on and formulated guides for the use of curare. It seemed well to study the action of the drug and to know the hazards and methods of overcoming untoward effects of the drug before using it. I would urge that any one who plans to employ curare first study all the phases of its use or have a skilled anesthetist familiar with its action at hand to administer the drug. The only report of an ophthalmic operation performed with the aid of curare which I have found was that of an enucleation (Baird [13]). No report of its use with local anesthesia in surgery of any kind was found.

Hazards of Cataract Surgery with Curare as an Aid to Local Anesthesia.—The drug was not tried without realization of the hazard of the development of respiratory paralysis with larger doses. Curare should be given only by those who have studied and are prepared to administer artificial respiration. Irreversible depression of the central nervous system due to anoxia must not be permitted to develop. Fortunately, overdosage is unnecessary in the use of curare in cataract surgery. Neostigmine methylsulfate, 0.5 mg., was ready for administration, and apparatus for artificial respiration and pulmonary insufflation with the use of an airway or intubation was at hand. Proper pulmonary exchange may not be adequately accomplished by manual artificial respiration. It may be done only with a pulmotor or with a gas-oxygen

6. Cole, F.: The Use of Curare in Anesthesia: A Review of One Hundred Cases, Anesthesiology **6**:48, 1945.

7. Whitacre, R. J., and Fisher, A. J.: Clinical Observations on the Use of Curare in Anesthesia, Anesthesiology **6**:124, 1945.

8. Adams, R. C.: Newer Anesthetic Agents and Methods, Kansas City M. J. **22**:11, 1946.

9. Gross, E. G., and Cullen, S. C.: The Effect of Anesthetic Agents on Muscular Contractions, J. Pharmacol. & Exper. Therap. **5**:521, 1914.

10. Fegler, J.: Action of Curare on Respiratory Center, J. Physiol. **100**:417, 1942.

11. Schmidt, C. F.: Recent Developments in Respiratory Physiology Related to Anesthesia, Anesthesiology **6**:113, 1945.

12. Macon, E. B., and Bageant, W. E.: Some Clinical Observations on the Use of Curare in Anesthesia, M. Ann. District of Columbia **16**:533, 1947.

13. Baird, J. W.; Johnson, W. R., and Van Bergen, F. H.: Pentothal-Curare Solution: A Preliminary Report and Analysis of Its Use in One Hundred and Sixty Cases, Anesthesiology **9**:141, 1948.

14. Harroun, P.; Beckert, F. E., and Hathaway, H. R.: Curare and Nitrous Oxide Anesthesia for Lengthy Operations, Anesthesiology **7**:24, 1946.

15. Shane, S. M.: Curare a Complement to Anesthesia, Anesth. & Analg. **24**:256, 1945.

bag connected with an apparatus or a pressure tank. Those who are not trained in resuscitation should have the curare given by an expert anesthetist.

Experience with Clinical Use of Curare.—Fortunately, in surgical procedures for cataract, the smaller doses of curare are sufficient for quieting or stilling the eye and the general muscles. The eye is not incised until danger of paralysis is passed. The peak of the effect of the intravenous administration of curare is reached two or three minutes after the injection is completed. If the condition is satisfactory at this period, respiratory embarrassment will not be experienced, and the surgeon may proceed expeditiously with the operation on a quiet eye in a quiet body. I had difficulty in only 2 cases. In 1 of them laryngeal stridor resulting from adductor cord paralysis was quickly relieved by neostigmine methylsulfate. In the other case, insufficient sedation permitted apprehension to increase on the development of respiratory depression, with resulting intraocular hemorrhage as a complication of high systolic and diastolic blood pressure. In a third case, in which the operation was done in my clinic by an assistant in my absence, artificial respiration for the period of action of the curare was needed.

Curare should not be used if the patient has had a recent disease of the upper respiratory tract or any condition in which an excess of secretion may collect in the absence of muscular ability to eject it. Its use is contraindicated in cases of asthma or emphysema. The drug may be administered with caution and in smaller doses to patients who have renal damage, in whom the ability to excrete the drug is diminished and its action thereby prolonged. All the drug is not excreted in the urine; some is destroyed in the body. Its use should be avoided in cases of uncontrolled hypertension, of emotional disorders and of senile degeneration. Curare has no direct effect on the heart or on the blood vessels except that with larger doses the blood pressure may rise as the respiration is depressed, then fall sharply as the respiration fails. Unless an overwhelming dose is given, the period of respiratory depression or paralysis which may possibly supervene should not be over five to ten minutes. Basal or general sedation and analgesia plus deep local anesthesia have minimized the dose of curare needed. Slow injection with constant attention to the sequence of muscular relaxation has added to the safety of its use and the absence of embarrassing events.

ANIMAL RESEARCH AND CLINICAL STUDY OF OPHTHALMIC PATIENTS IN ANTICIPATION OF OCULAR SURGERY

In order further to elucidate the indications, actions and methods of use of curare for cataract surgery, preliminary tests were conducted on rabbits by Dr. Donald Hughson, who observed that unconscious animals to which thiopental alone had been given intravenously were

still able to respond by kicking when held up and their hind feet allowed to touch the table, whereas they were flaccid after the additional injection of curare. It was interesting that the amount of curare required to produce flaccidity was considerably less (one third) when the drug was combined with thiopental than when used alone. The value of experimental ocular surgery on animals was evident. Hughson observed that paralysis of the muscles around the animal's nose and eyes preceded the head drop used in standardization of the drug. The decrease in intraocular tension recorded by Duke-Elder in experiments with curare was confirmed by Hughson.

In a study of intraocular tension in 29 cases of cataract in which I operated, Hughson recorded an average decrease of 3 mm. of mercury. Curare had little, if any, effect in a case of glaucoma. It must be recorded that I used only relaxing, not paralyzing, doses of curare in these cases. Clinical research in preparing patients for operation was conducted by Dr. John Roche, under my direction, in the department of ophthalmology of Bellevue Hospital. The purpose was to determine the approximate average dose required (1) for ptosis and for quietude of the eye and general voluntary muscles, (2) the dose required for abolition of ocular movements on command and (3) the dose at which respiratory depression might be experienced, and thereby avoided. Members of the department of anesthesiology, under the direction of Dr. E. A. Rovenstine, were most cooperative in being on hand, ready for any emergency. Dr. Roche's report will be published separately. In general, the dose required for quietude of the ocular muscles was minimal, much less than that for abolition of motion or command. The third phase was not investigated thoroughly, as there was no point in going to this limit, but it was well beyond the point of abolition of ocular movements on command. Patients who have had preliminary tests without any untoward event may well be given the therapeutic dose of curare for their cataract operation on the following, or on any successive day.

RATIONALE OF USE OF CURARE IN THE PRESENT SERIES OF CATARACT EXTRACTION

I first became interested in the clinical use of curare in cataract surgery a little over two years ago. Patients were given sedation, local anesthesia and palpebral akinesia; then they were observed. If they were found to be still hyperkinetic, curare was given intravenously in the form of intocostrin.* Aware of the reports that the ocular muscles were affected first, I decided to use less than the minimal dose (not over 9 mg.) for any patient over 150 pounds (68 Kg.). There is no point in injecting curare locally, as is done with procaine in the Van Lint or the O'Brien method of palpebral akinesia or by retrobulbar

injection, for even though it were active locally, one would only be perpetuating the fallacy of the local preparation for cataract surgery and neglecting the general preparation of the patient through general akinesia. The therapeutic dose recommended in shock therapy, as being within the limits of safety, is ½ unit per pound of body weight for persons with weak musculature and up to ¾ unit (both totals are reduced by 20 units) for persons with musculature of average strength. It was realized also that the hyperkinesia was a deep reflex produced by apprehension and surgical manipulation; so an effort was made to improve the basal sedation and analgesia in previous use. Amobarbital sodium (sodium amytal®), bromides and paraldehyde were used no longer. Chloral hydrate and phenobarbital were retained, and pentobarbital sodium was used in place of amobarbital as being more uniform and reliable. Considerable satisfaction has been experienced with the use of phenobarbital sodium when necessary by injection in the last hour before operation. Meperidine has been found excellent for basal analgesia in the injection of 50 mg. intramuscularly one hour before operation and the addition of as much as 50 mg. intravenously on the operating table if needed. The dose of all agents is graduated according to the patient, his condition and his reactions. More recent experience has shown that the percentage of cases in which curare is required is lessened with the improved sedation and analgesia, although the basic need for it remains in all because there remains the deep reflex of contraction of voluntary muscle, even under profound sedation, sufficient to induce sleep.

The administration of curare has been found indicated if, after an adequate dose of sedatives and analgesics, and with the use of deep local anesthesia and palpebral akinesia, the patient still moves his eyes, still squeezes the fellow eye, thereby rolling upward the eye to be operated on, still has rigidity of the neck or skeletal muscles or still has respiratory neurosis. The effects of curare should be obtained, the peak determined and the level of safety established before the eye is incised. For this reason, the intravenous is preferred to the intramuscular route. The effect and the timing can be more accurately determined. In case a satisfactory vein for intravenous use cannot be reached through the puncture in the skin, it is well to tell the patient that the assistant will make a small incision with local anesthesia for direct exposure of the vein and easier injection. A skilled assistant or the anesthetist injects 20 units of intocostrin® or *d*-tubocurarine intravenously over a period of one minute, then pauses while the surgeon makes further observations. The fellow eye is exposed, and the patient is instructed to keep both eyes open. Ptosis is to be distinguished from closure of the eyes due to somnolence induced by the sedatives. Patient with ptosis due to curare is unable to lift the upper lid on command, but may retain the ability to raise the brows and corrugate the

forehead for some time after ptosis develops. The blepharostat is retained in the eye to be operated on, and the cornea is kept moist with saline solution. If ptosis of the lid of the fellow eye and stilling of the orbicularis muscle of the fellow eye and the motion of the eyes do not develop, an additional 10 units of the solution is injected, thirty seconds being taken for the process, and observations are repeated. If the phenomena develop, a test is made for muscular rigidity by the surgeon's moving the head from side to side. If the neck has become relaxed, the effect is sufficient and the injection may be stopped. If not, another 10 units is injected and the analysis repeated. The time interval is increased with an additional dose. The effect and development of muscular relaxation on intravenous injection of curare are rapid, and complete body distribution requires only two to three minutes. Now that 40 units has been given, a pause of at least one minute is made before the decision is made to inject more. The patient is reassured by the surgeon as the observations progress; but, contrary to my original idea, it is better not to test his ability to take a deep breath, as he may discover his general muscular asthenia and become apprehensive over this feature. It is better to observe his respirations and to be content if they are regular, even though shallow and decreased in number. If the patient is well developed, young and in good condition, a fifth, or even a sixth dose of 10 units may be injected. This is as far as I have gone in the use of the drug for this purpose.

CENTRAL DEPRESSANT OR SEDATIVE ACTION OF CURARE

Most observers who have used curare in the human subject have not reported any depression of the central nervous system or sedative action. The conditions of its use in combination with general anesthesia may have precluded the observations. Berman observed central sedation. I have observed that with local anesthesia, when sedation induced with barbiturates and meperidine was insufficient to produce general relaxation and sleep, the patient became more generally quiet with curare, and even went to sleep, snoring quietly, soon after the drug was injected. It cannot be said that at this time the peak of the other sedatives had been reached. This relaxing and sedative effect of curare, if it exists, is better than that which might be obtained with larger amounts of barbiturates and meperidine. In a very few of my patients I found that I might have given them more curare, or repeated the injection, as the rigidity and ocular movements returned too soon. Usually after one dose has been finished, a delay of two to three minutes is made to permit the drug to reach the peak of its action. Then, if nothing untoward has developed, the operation may safely be proceeded with, the period of muscular relaxation lasting fifteen to twenty minutes, during which period the operation for extraction of the cataract may be finished.

CONDUCT OF THE OPERATION

The time spent in this preparation, a total of two to six minutes for the injection and two to three minutes for the final observations for safety, is well repaid in the expedition possible in the surgical manipulation. The patient stops talking and need not be talked to, except to be reassured that all is going well. He need not be told repeatedly to look down or to keep his other eye open. His body is relaxed. The eyes remain quiet and steady in the primary position. Nystagmus due to congenital amblyopia with complicated cataract, present in 2 of the patients, was completely abolished for a period of sixteen minutes in one and of twenty minutes in the other. It is not necessary to use a superior rectus suture. The patient may be able to move, and can move, his eyes on command, but it is better not to have to tell him to move them. It may be repeated that the dose required to abolish movement of the eye on command is greater than that necessary for quiet. Only the latter phase is desired, and the dose required is well within the safe limits of the drug. Recovery from the effects of single minimal doses of curare is smooth and uneventful. It is not necessary to use neostigmine. Muscular function returns, and even on inquiry no complaint is made of the experience. Some sedative-like clouding of the sensorium may be added to the effects of the other sedatives.

SURVEY OF CASES IN WHICH CURARE WAS USED IN CATARACT SURGERY

Intocostrin® or *d*-tubocurarine has been used in over 100 cases within the past two years. Patients cannot be grouped as surgical entities; the factors are too variable. Even though I had rounded out the series to 100 cases, I should not attempt to give exact percentages or statistics, for this might lead to erroneous conclusions. At best, I can give only my personal experiences and impressions, based on a critical review of the cases in which curare was indicated and used. The patients selected were those who exhibited hyperkinesia after all other efforts for relaxation had been made. The ratio of male to female patients for whom curare was used was 3:2. The emotional status of the female is usually greater than that of the male, but the female may require less sedation and analgesia than the male and be less apprehensive over the cataract operation and its result than the male, who is more worried over his ability to return to his vocation. The ages of the patients varied from 24 to 82 years. One was in the third decade of life; approximately 14 were in the fourth decade; 14, in the fifth decade; 24, in the sixth decade and 40, in the seventh decade or beyond. The percentage of cases of the last group in which curare is indicated is less than in the younger groups. However, the effects of apprehension are evident even in the elderly group. The use of curare is a new approach to the relief of muscular spasm and the production of akinesia in cataract surgery.

Dose of Curare Employed.—In beginning the use of the curare, I frequently used 60 units. Later I found 6 to 7.5 mg. of intocostrin* or *d*-tubocurarine sufficient for most patients. Approximately 40 per cent received 9 mg.; 20 per cent received 7.5 mg (50 units), and 40 per cent received 40 units (6 mg.). Judged by the quieting effect, these doses were sufficient in all but 10 of the cases. In the 10 cases mentioned general akinesia did not develop, and the palpebral ocular and general rigidity and spasm were retained to a less degree, causing embarrassment during the operation. In 3 of these cases vitreous was extruded. This record of loss of vitreous in a series of patients who were manifestly poor risks from this standpoint to begin with is favorable as compared with 4 to 6 per cent in a previous unselected series without curare. In fact, when considered in relation to the probable loss of vitreous in patients with uncontrolled rigidity and muscular spasm, the results obtained in the present series was satisfactory to me.

GENERAL ANESTHESIA WITH INTRAVENOUS INJECTION OF THIOPENTAL SODIUM (PENTOTHAL SODIUM*)

Some hypertonic patients will not quiet down sufficiently to permit operation with local anesthesia. The amount of medication needed, combined with the fear neurosis, would be great enough to induce unfavorable reactions, nausea and vomiting. My associates and I use thiopental sodium intravenously, not because we feel safe from a fatality with it, but because it is accepted and is the best one has at present. If anoxia is prevented and an experienced anesthetist is employed, thiopental anesthesia may be pleasing, both to the surgeon and to the patient. I have been pleased with the position of the eyes and the relaxation during the anesthesia and have been surprised at the lack of unfavorable reactions in the period of recovery. We are still hoping for a safer drug or combination of drugs.

All cataract surgeons have had patients who manifestly had emotional disturbances of such intensity as not to be overcome safely without general anesthesia. Particularly with one-eyed patients, the amount of sedatives and analgesics required might be such that complications in recovery would seem certain. I have employed a general anesthetist to administer thiopental sodium intravenously to such patients and in general have been pleased with the results. However, with some patients a deep plane of anesthesia is necessary to overcome rigidity. For these, the reports of Davison and Letton[16] and Baird[15] on the combination of curare and thiopental are encouraging.

With a barbiturate alone, induction of anesthesia is generally pleasant and rapid, but muscular relaxation is poor, at least with a dose

16. Davison, T. C., and Letton, A. H.: Muscular Relaxation in Abdominal Surgery with the Use of Pentothal, Oxygen and Curare, South. Surgeon **13**:437 1947.

which can be considered safe for the patient. This has been an obstacle to expansion of the use of intravenous anesthesia with such short-acting barbiturates as thiopental, pentobarbital and hexabarbital (evipal®). Severe laryngospasm and other reflex activities, which easily occur under barbiturate anesthesia, have been additional disadvantages. A dose sufficient for third plane, third stage anesthesia produces true muscle relaxation but also profound depression of the cerebrum and medulla.

Concomitant use of curare removes these limitations. Curare has made it possible to produce anesthesia by intravenous administration of barbiturates for major surgery without resorting to a deep plane anesthesia. The combination offers many advantages for abdominal surgery, neurosurgery, bone and joint surgery, genitourinary surgery and numerous other operative procedures of many hours' duration.

From an extensive experience, Davison and Letton concluded that the addition of curare diminished the amount of thiopental required by 26.3 per cent. This made it possible for patients to undergo even very extensive operations without the dangers attendant on deep anesthesia. As these authors saw it, curare supplements the inability of thiopental to produce relaxation, and thiopental supplements the inability of curare to produce anesthesia. Thus an acceptable combination is formed, and one which has few objectionable features.

There are two ways of administering the thiopental-curare combination. The first utilized a mixture of the two agents in fixed ratio; with the other, curare may follow the barbiturate. A precipitate is formed when intocostrin® or *d*-tubocurarine chloride solution, both of which are acid in reaction, comes into contact with the basic thiopental sodium. This precipitate is soluble in an excess of thiopental sodium or plasma and has usually been allowed to enter the blood stream if the quantity was small, as it is when curare and barbiturate are given alternately through the same needle.

With the method of direct injection of a mixture of fixed ratio, as proposed by Baird, *d*-tubocurarine chloride solution containing 20 units per cubic centimeter or, better still, the more concentrated preparation, containing 100 units per cubic centimeter (high potency *d*-tubocurarine chloride solution), should be used. These products have a lower total acidity than intocostrin® and permit preparation of mixtures of thiopental and curare of optimal ratios without precipitation. In addition, with high potency *d*-tubocurarine chloride solution, significant dilution of the thiopental stock solution is avoided.

From the point of view of precipitation the maximum practical limits of curare concentration in 1 cc. of 2.5 per cent thiopental solution are 10 units of high potency *d*-tubocurarine chloride solution or 7.5 units of regular potency *d*-tubocurarine chloride solution. Baird found a

mixture of 5 units of *d*-tubocurarine chloride and 25 mg. of thiopental sodium in 1 cc. of solution most useful, producing optimal results for his purpose.

SUMMARY AND CONCLUSIONS

For the delicate manipulations of cataract surgery, a quiet eye, a quiet patient and a quiet surgeon are desirable. Fear, apprehension and pain produce deep physiologic reflexes, which result in local and general rigidity and spasm of the voluntary muscles, known as hyperkinesia.

Surgeons have sought by proper psychologic approach, and by the use of sedatives, analgesics, local anesthesia and palpebral and orbital akinesia, to produce the desirable state of relaxation in the patient with cataract. The average patient responds well to this approach. About 15 to 20 per cent, however, may still exhibit the effects of abnormal muscular action after the safe dose of the various drugs has been administered. For these, the use of curare in the form of the purified extract or crystalline salt in minimal dose has provided, with local anesthesia, the muscular quiet which has made it possible for them also to achieve mental relaxation. The amount needed for stilling of the muscles is much smaller and safer than the dose required for abolition of movement on command.

I am the first to use curare in combination with local anesthesia for cataract extraction. I was attracted to its clinical trial by the published, and verified, reports that the first action of the drug is on the ocular muscles, producing in progression an effect similar to that of myasthenia gravis. I have been well aware of the dangers of the drug, but, fortunately, with proper precautions, I have had no embarrassing complication. Those who wish to try the action of curare are advised to do so only with the aid of a skilled anesthetist, and not to incise the eye before the peak of the effect of the injection has passed, within three minutes after the injection is finished.

Experience with the use of curare has been most satisfactory for cataract extraction. It is a definite addition to the surgeon's armamentarium in the approach to uneventful and successful cataract extraction in difficult cases. Relaxation of the patient helps in the relaxation of the surgeon.

There are patients, particularly those with only one eye remaining, who are not suitable subjects for surgical procedures with local anesthesia. For these, thiopental combined with curare, the latter being used before the operation has begun, seems to offer better promise than thiopental alone. Again, it may be advised that the injection of curare be finished before the incision in the eye is made.

Clinical research on the use of curare in conjunction with local anesthesia in cataract extraction is still in progress. This is a new approach to the relief of muscular spasm and the production of akinesia in cataract surgery.

ABSTRACT OF DISCUSSION

Dr. Frederick C. Cordes, San Francisco: Some of the pioneer work on the use of curare in anesthesia was done at the University of California Medical School by Harroun, Beckert and Hathaway, and the first use of curare in anesthesia for thoracic surgery was reported from this school by Stephens, Harroun and Beckert. However, my experience with the drug is limited.

Curare does not produce analgesia or sedation; so its use is limited to those cases in which muscular relaxation is desired. The ocular muscles are the first to be affected, and therefore the amount of drug necessary to produce the desired effect is much less than the usual dose employed in general surgery. This fact helps to justify its use in ophthalmology. When curare is used, it should be given only by one familiar with the drug.

In my limited experience, I feel that curare has no place in the average cataract extraction, in which local anesthesia, akinesia and sedation are effective. I agree with Dr. Kirby that when these measures fail and the patient is unruly and uncooperative and rolls his eyes, the use of curare may be the saving factor in the success of the operation. The value of curare in selected instances can be illustrated by my experience in one of my cases. In my opinion, it is also indicated in the case of the hard of hearing patient and of the foreigner who has language difficulty.

The patient, a man aged 41 with myopia of 16 D., had anterior and posterior cortical opacities, with vision reduced to 20/200 in each eye. Mild nystagmus was present. After sedation and the use of local anesthesia and akinesia, the patient was still very apprehensive, squeezing the lids and rolling his eyes; in fact, he requested general anesthesia. Sixty units of *d*-tubocurarine was given intravenously. Within a short time there were choking, gagging, nausea, dysarthria and considerable distress, due to sudden accumulation of pharyngeal secretions beyond the control of the patient. The patient was reassured and told to breathe quietly, and within two minutes he had quieted down and he remained relaxed during the rest of the operation.

The operation was difficult and necessitated the use of the erisophake to remove the lens. The zonule was resistant, and it required a good deal of time gradually to break the fibers. The lens was removed; the sutures were tied, and the operation ended without complications. During this lengthy procedure the lids were relaxed, and the eye was immobile, even all traces of the nystagmus having disappeared.

In the limited number of cases in which I have used the drug, I have encountered no difficulties. I have, however, observed that the eyes seem to be softer than normal. In 4 cases, 3 of repair of squint and 1 of enucleation, in which curare was used to facilitate the intubation, there seemed to be increased bleeding.

Curare has no place in the average cataract extraction but is of great value in cases which come within the indications established by Dr. Kirby. I have found the method of giving the drug and the dose as outlined by Dr. Kirby satisfactory.

The use of the drug is not without danger. As has been pointed out, it is contraindicated, or to be used with caution, in cases of myasthenia gravis. When it is to be used, it should be given only by a skilled anesthetist who is familiar with its uses and who will stand by during the operation prepared to give the proper type of artificial respiration should it become indicated.

DR. W. B. CLARK, New Orleans: When my associate, Dr. William McDonald Boles, returned from service in the Mediterranean Theater with the United States Army Medical Corps, he was enthusiastic over the advantages of thiopental (pentothal*) sodium for ophthalmic surgery and suggested that curare be combined with it for operations on young adults. Our preliminary experience was satisfactory; a considerable reduction in the amount of thiopental sodium was necessary. We extended the use of curare to cases in which basal and local analgesia were to be used. Our first experiences were disappointing because we limited the dose of curare to 20 units per patient; we then realized that some patients require more and that the dose must be individualized. We then began to have gratifying results.

Our method is simple. The retrobulbar injection of procaine hydrochloride is made in the usual manner except that one-half the amount previously used, or 1 cc., is injected before the patient's face is prepared and before we scrub. At the same time an infusion of isotonic solution of sodium chloride is begun into the ankle vein, the rate being about 40 drops per minute until the conclusion of the procedure. It has been explained to the patient that the objective of all these maneuvers is to save him pain. Akinesia or local analgesia is administered as desired. Then, just before the section is made, the 20 units (1 cc.) of curare is injected into the infusion tubing, at the rate of 10 units per minute. The injection is made from a syringe which has previously been loaded with 60 units (3 cc.) of curare. The original injection is often sufficient to keep the patient's eye quiet during the entire operative procedure. If, however, there is any motion, voluntary or otherwise, the circulating nurse, at a signal previously arranged, injects additional curare as necessary; not more than 10 units is given at each injection, and the rate is the same as for the original injection.

We have administered as much as 80 units of curare at a cataract operation, and while we keep a syringe filled with neostigmine for immediate use, it has never been necessary to administer the latter drug. We have used this method in patients of various ages, ranging from 30 to 92 years. It has been employed in all varieties of intraocular surgery but has proved most generally helpful in cataract extractions and in keratoplasties.

Loss of well formed, viscid vitreous has become an infrequent accident in our practice since we have adopted this form of anesthesia. We think the method has been extremely beneficial to the patient, and I can testify that it has been good for the ophthalmic surgeon. While I am operating under the form of anesthesia I have described, I can give the patient all of my attention.

DR. DANIEL B. KIRBY, New York: I certainly agree that reassurance of the patient before the operation is extremely important; but once the operation has started with the proper sedation and analgesia and curare, it is not necessary to do much talking to the patient.

I agree with Dr. Cordes that administration of atropine and scopolamine before the operation is an excellent adjuvant to the use of the curare. It helps to reduce the secretions, which may be bothersome.

I have not found the eye embarrassingly soft. The tension, as recorded, falls 3 to 5 mm. of mercury.

I should like to stress again the importance of finishing the injection of curare and of establishing the peak effect within two or three minutes after the injection is finished, and before the eye is opened.

A year ago I told Dr. James Allen and his associates about the use of curare, and he has since used it in over 70 cases. He said that I might quote him as saying that certain patients, particularly 6 whom he had in mind, who had been prepared in the routine way and on whom operation was impossible because of their demeanor and behavior, were turned over to him, and that he was then delighted with the manner in which he was able to bring them out of their difficulty with the use of curare. He attributed his success to the use of curare in those cases.

RETROLENTAL FIBROPLASIA

A Clinical Study of Two Hundred and Thirty-Eight Cases

MERRILL J. KING, M.D.
BOSTON

THE TERM "retrolental fibroplasia" was devised in 1941 by Dr. Harry H. Messenger, of Boston, for use by Dr. Theodore L. Terry.[1] Terry[2] applied the name to an ocular disease syndrome in which, as he stated, vascularized embryonic tissue develops behind the crystalline lens of the eye. Previously, in occasional cases the disease had been reported, under various names, as a rare congenital malformation which was usually observed shortly after birth in full term infants, as a rule only one eye being involved. It was Terry[3] who, in 1942, first associated retrolental fibroplasia with prematurity. He[2] summarized the syndrome as follows:

> The typical characteristics of the disease are opaque vascularized membrane behind the lens, microphthalmia, shallow anterior chambers, fetal-blue color of iris, thin ciliary processes in front of the opaque tissue, searching nystagmus, apparent photophobia, persistent hyaloid artery and often retinal separation.

In his series of 117 cases of retrolental fibroplasia only 8 were of infants born at full term. His belief that the syndrome is not congenital but develops postnatally was based on the fact that in 3 prematurely born infants whose eyes he had found to be normal shortly after birth he subsequently found well established retrolental fibroplasia. He stated the belief that the disease was due to embryonic connective tissue which developed in the meshwork of a persistent tunica vasculosa lentis and stated[2]:

> The basis of the disease lies in the presence of a functioning hyaloid artery and tunica vasculosa lentis in all infants born three to four weeks prematurely.

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From the Department of Ophthalmology, Harvard Medical School, and the Massachusetts Eye and Ear Infirmary.

Read before the Section on Ophthalmology at the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June 9, 1949.

1. Terry, T. L.: Fibroplastic Overgrowth of the Persistent Tunica Vasculosa Lentis in Premature Infants, Arch. Ophth. **29**:36-53 (Jan.) 1943.

2. Terry, T. L.: Ocular Maldevelopment in Extremely Premature Infants: Retrolental Fibroplasia; General Consideration, J. A. M. A. **128**:582-584 (June 23) 1945.

3. Terry, T. L.: Extreme Prematurity and Fibroplastic Overgrowth of Persistent Vascular Sheath Behind Each Crystalline Lens, Am. J. Ophth. **25**:203-204 (Feb.) 1942.

In his last paper Terry [4] said: "At present, the name retrolental fibroplasia is applied to the abnormality in both premature and full term infants." However, he further stated that it occurred much more frequently in prematurely born children.

At present there is considerable confusion in the literature as to a suitable name to be applied to this disease. The Owenses,[5] Kinsey and Zacharias,[6] Unsworth [7] and Clifford and Weller [8] stated their adherence to the term retrolental fibroplasia. Reese and Payne,[9] however, designated the condition as "persistence and hyperplasia of the primary vitreous." Krause [10] called the disease "congenital encephalo-ophthalmic dysplasia." Although all these terms may be criticized, I shall use, for reasons of convenience, the name retrolental fibroplasia.

ETIOLOGY

The cause of retrolental fibroplasia is still unknown. Prematurity and weight at birth are predisposing factors in a large majority of cases. There is no doubt that the incidence of the disease has increased in the last decade, and much more so in the last five years. The incidence appears to be greater in certain cities and localities than in others. It is evident that this increase is not accounted for by the failure to diagnose the disease in previous years. Kinsey and Zacharias [6] and Dunham [11] pointed out that the increase is not due primarily to a significant increase in the survival rate of premature infants.

Terry [4] emphasized the importance of a reopening of a few of the vessels of a persistent tunica vasculosa in the development of the disease. Reese and Payne [9] stated that the lesion is due to persistence and

4. Terry, T. L.: Retrolental Fibroplasia, in Levine, S. J.; Butler, A. M.; Emmet, L., Jr., and Weech, A. A.: Advances in Pediatrics, New York, Interscience Publishers, Inc., 1948, vol. 3.

5. Owens, W. C., and Owens, E. U.: Retrolental Fibroplasia in Premature Infants, Tr. Am. Acad. Ophth. **53**:18-38 (Sept.-Oct.) 1948.

6. Kinsey, V. E., and Zacharias, L.: Retrolental Fibroplasia; Incidence in Different Localities in Recent Years and a Correlation of the Incidence with Treatment Given the Infants, J. A. M. A. **139**:572-578 (Feb. 26) 1939.

7. Unsworth, A. C.: Retrolental Fibroplasia: A Preliminary Report, Arch. Ophth. **40**:341-346 (Sept.) 1948.

8. Clifford, S. H., and Weller, K. F.: The Absorption of Vitamin A in Prematurely Born Infants with Experience in the Use of Absorbable Vitamin A in the Prophylaxis of Retrolental Fibroplasia, Pediatrics **1**:505-511 (April) 1948.

9. Reese, A. B., and Payne, F.: Persistence and Hyperplasia of Primary Vitreous, Am. J. Ophth. **29**:1-19 (Jan.) 1946.

10. Krause, A. C.: Congenital Encephalo-Ophthalmic Dysplasia, Arch. Ophth. **36**:387-444 (Oct.) 1946.

11. Dunham, E. C.: Premature Infant, Bureau Publication, no. 325, United States Department of Labor, Children's Bureau, 1948.

hyperplasia of angioblastic remnants of the primary vitreous. They expressed the belief that the condition is congenital. Krause [10] also stated that the disease is congenital and, further, found associated abnormality of the cerebral and the retinal neuroectoderm. Unsworth [7] stated that retrolental fibroplasia in premature infants is not congenital, but is a postnatal development in which the retinal vessels play a prominent role.

In a recent article Kinsey and Zacharias [6] presented suggestive evidence that medication used postnatally may be of etiologic significance. They found that in certain areas the incidence of retrolental fibroplasia has increased significantly in recent years. In Boston, where the data are most complete, the rise in incidence was found chiefly in infants of the 3 to 4 pound (1,360 to 1,815 Gm.) weight group. The greater frequency of retrolental fibroplasia correlates with several changes in treatment of premature infants, i. e., the use of vitamin supplements in water-soluble form and the increased use of iron. While they pointed out that a positive correlation between a rise in the incidence of the disease and changes in treatment does not constitute proof of any causal relation between the two, it may, nevertheless, have etiologic significance.

Owens and Owens,[8] who are the first to have observed the development of retrolental fibroplasia, watched its development in 9 premature infants. The abnormality appeared in these infants between the second and the fifth month; all visible remains of the hyaloid system had disappeared before the onset of the disease. In these infants the initially normal fundus picture was replaced by angiomatous dilatation of the retinal vessels, followed by massive retinal exudation, retinal detachment and the formation of a retrolental fibroplastic membrane.

More recently, Owens and Owens [12] postulated that retrolental fibroplasia may be caused by a vitamin E deficiency in the infant. Preliminary studies on a small series of premature infants have supported this thesis.

CLINICAL OBSERVATIONS

The data presented in this paper are based on the findings in a series of 238 patients all of whom showed retrolental fibroplasia, according to the classic description of Terry. This series includes Terry's original 117 patients and 121 additional patients. Many of the patients have been followed for from two to four years and a few for at least seven years. Twenty-eight of the patients have been dropped from the group, for various reasons. Therefore in some of the final follow-up studies they, of necessity, will not be included. All of the remaining patients

12. Owens, W. C., and Owens, E. U.: Vitamin E Studies in Relation to Retrolental Fibroplasia, read at the eighth clinical meeting of the Wilmer Residents Association.

have been seen regularly, the younger patients at two month intervals and the older ones at six month intervals. When complications have arisen, the examinations have been much more frequent.

All the infants had well developed retrolental fibroplasia when they were first seen by us; the early development of the disease therefore cannot be described.

Retrolental fibroplasia is almost always bilateral; it may, however, be much more extensive in one eye than in the other. Typically, by the time of full development of the disease (from the fourth to the sixth month after birth) there is a varying amount of microphthalmos, because the eyes fail to grow normally as the membrane develops. It is interesting that an eye with a complete membrane is usually smaller than a fellow eye with an incomplete membrane. Nystagmus or nystagmoid movements are consistently present and are usually exaggerated when the eye is exposed to light. These movements persist as long as the child is able to perceive light; as a rule, they gradually lessen or cease with the development of total blindness. Strabismus, usually of the convergent type, is frequently present. Characteristically there is a tendency to press or rub the eyes. This is apparently a protective reflex in response to physical, as well as to psychologic, stimuli. The conjunctivas are usually white unless glaucoma, conjunctivitis or iritis is a complicating feature. The anterior chamber is usually shallow, and in advanced cases it is often flat. The pupils may or may not react to light. The motility of the iris is influenced by pressure of the crystalline lens, which has been displaced forward by the retrolental membrane. The pupillary margin may be bound down by posterior or anterior synechias. The iris is characteristically poorly developed, usually having the fetal blue or grayish blue color described by Terry. The pupillary membranes have in large part disappeared by the time the retrolental fibroplasia is complete; however, it is not unusual to see fine bands stretching across the pupil. Dilated and new-formed vessels are often present in the iris. Foci of atrophy of the iris are not infrequent in the later stages. Fine opacities may be present in the cornea. As a rule the lens is clear. Occasionally there may be small posterior lenticular opacities; complete opacification of the lens may occur after the development of a retrolental membrane. In cases of well developed retrolental fibroplasia the opaque, grayish white, vascularized membrane can be seen lying against the posterior surface of the lens. In premature infants it is usually bilateral, whereas in infants born at term it may be unilateral. The membrane may be complete, covering the entire visible area of the posterior surface of the lens, or it may be partial. In the latter condition the membrane is often triangular, with the base of the triangle placed peripherally in the region of the pars plana and ciliary body and the apex extending back into the vitreous, frequently toward the optic disk. In

such cases the membrane is usually on the temporal side. It is not unusual to have a complete membrane in one eye and a partial membrane in the fellow eye. Actually, in some cases the membrane may be very fine and limited in extent, appearing as a nebulous, grayish collaret in the extreme periphery in the region of the pars plana. These fine membranes can sometimes be seen only by indirect ophthalmoscopy through widely dilated pupils. The membrane may vary in density throughout its extent. In cases of incomplete membrane formation, bands are frequently seen extending between the fibroplasia and the retina. Localized areas of retinal detachment may be present. Often these areas are seen in the early stages and disappear in the later stages of the disease. More frequently, however, these retinal folds and detachments persist. My colleagues and I have observed detachments which remained essentially the same for five or six years; however, after several years a total detachment may suddenly occur. As the child advances in age, the membrane may thin out or, in rare instances, contract. The blood vessels in the retrolental membrane may in time become attenuated and may practically disappear in the older patient. It is not unusual to see localized hemorrhages on the membrane even as late as the twelfth month of life. Vitreous and retinal hemorrhages, and even hyphema, may likewise occur in the late stages, long after the development of the retrolental membrane. These hemorrhages have occurred in some of our cases as late as at 4 years of age.

Elongated ciliary processes are frequently observed in the extreme periphery if sufficient dilation of the pupil can be obtained.

When the membrane is partial, the vitreous may be seen to contain floating opacities. In a few patients a persistent hyaloid artery has been observed. They were not seen frequently enough, however, to indicate that the membrane was formed from a "reopening of the hyaloid system."

The fundus, when it can be seen, usually shows degenerative changes in the retina, especially in the macular region. Foci resembling healed chorioretinitis are occasionally present. Pallor of the nerve head is not uncommon. Retinal folds and detachments are usual; retinal hemorrhages are occasionally observed in well advanced cases.

INCIDENCE

Studies have shown that the incidence of retrolental fibroplasia varies for different localities and for different hospitals in the same locality. This has been brought out in a recent paper by Kinsey and Zacharias,[8] who reviewed the literature and added extensive data of their own. They could establish no definite reason, or reasons, for this variation in incidence. They also showed that the incidence has increased in some places in the past few years. They pointed out that this increase is especially true among infants weighing 3 to 4 pounds at

birth. Similarly, the literature indicates that retrolental fibroplasia has occurred more frequently in certain hospitals in Boston, Hartford, Conn., and Providence, R. I., than in certain hospitals in New York city and Birmingham, England. It must be pointed out that the occurrence of retrolental fibroplasia as gathered from the literature is based on reports from specific hospitals. It is possible, therefore, that these reports present an incomplete account of the occurrence of retrolental fibroplasia in any one locality.

Since the patients in our series were referred to us from many localities and came from thirteen states, the District of Columbia, Italy and the West Indies, the data are relevant only as regards the incidence in relation to weights at birth. Chart 1 shows a plot of the birth weights of the 228 infants in our group who were born prematurely. One hundred and ninety-four (85 per cent) of these infants weighed less

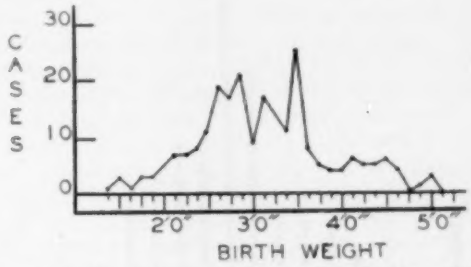


Chart 1.—Distribution of premature infants according to weights at birth, expressed in pounds and ounces.

than 4 pounds (1,815 Gm.) at birth; 101 (44.2 per cent) weighed less than 3 pounds (1,360 Gm.), and 34 (15 per cent) weighed from 4 to 5 pounds (1,815 to 2,268 Gm.) at birth. None weighed more than 5 pounds. These data are in agreement with those reported by Kinsey and Zacharias,[6] Owens and Owens[5] and Unsworth,[7] showing that retrolental fibroplasia occurs most frequently in premature infants whose weight at birth is less than 4 pounds.

We have found no evidence to indicate a hereditary factor in retrolental fibroplasia, nor were any social factors apparently responsible. In this series retrolental fibroplasia occurred in more than one member of a single family only in cases of multiple births. There were 54 instances of multiple births—52 sets of twins and 2 sets of triplets. Of the 52 sets of twins in our group, one infant in each of 22 sets died at birth or shortly after. Retrolental fibroplasia was present in both twins in 8 sets, whereas it developed in only one twin of each pair in 18 sets. In the remaining 4 sets of twins myopia and other degenera-

tive changes were present in the twin in whom definite fibroplasia did not develop. In 1 set of triplets, retrolental fibroplasia developed in both the infants who survived. In the second set of triplets one infant died at birth, one had retrolental fibroplasia and the eyes of the third were not affected.

Hess, Mohr and Bartelme [13] stated that the multiple pregnancy is the commonest cause of prematurity; one would, therefore, expect a high incidence of multiple births in our series of 228 infants, all of whom were born prematurely. Hess and his associates [13] also stated that twinning occurs in about 16 per cent of all premature births. Multiple

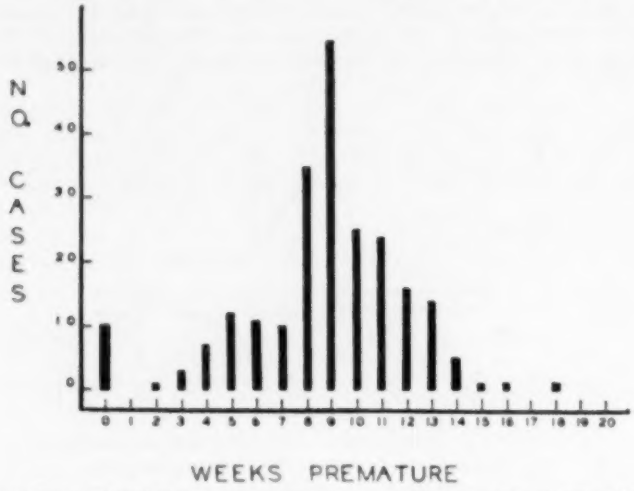


Chart 2.—Distribution of premature infants, according to week of birth before term.

births occurred in 54, or 24 per cent, of our series of 228 pregnancies which terminated prematurely.

Of the patients, 149 (65 per cent) were males and 80 (35 per cent) were females, a ratio of nearly 2 males to 1 female. The white race definitely predominated in our series. There were only 2 Negroes in the group, and they were twins. This racial distribution is not significant, since most of our patients were from New England, where the Negro population is relatively small.

13. Hess, J. H.; Mohr, G. J., and Bartelme, P. F.: The Physical and Mental Growth of Prematurely Born Children, Chicago, University of Chicago Press, 1934.

The period of gestation is often difficult to estimate accurately. From the information gathered from the parents and their obstetricians, we were able to get aceptable data on 221 of the 228 premature infants in our group. The birth weights of the 7 infants concerning whom we could not obtain satisfactory information, however, left no doubt that these infants had been born prematurely. One hundred and seventy-seven (77.6 per cent) of the patients were born from eight to eighteen weeks prematurely. Chart 2 indicates that 55 (24 per cent) of the infants were born in the ninth week before term, this being the highest occurrence of births in any one single week. The graph further indicates that 139 (61 per cent) of the infants were born in the period covering the eighth through the eleventh week before term.

The cause of prematurity is often obscure. Except for the relation to multiple births, no one cause was sufficiently common in our series to be significant.

There was a history of maternal bleeding during gestation in only 25 of the pregnancies in our series. Our data indicate that maternal disease during pregnancy has no bearing on the occurrence of retrolental fibroplasia in the offspring. The Rh factor, likewise, was not found to have any significance. To the best of our knowledge, rubella occurred in only 1 pregnancy, and this was not until the fourth month of gestation. The infant in this case was born six weeks prematurely and weighed 4 pounds 13 ounces (2,183 Gm.). When he was first seen by us, at the age of 6 months, he had fully developed retrolental fibroplasia with a complete membrane in each eye. The congenital anomalies usually associated with rubella were not found.

Evidences of toxoplasmosis were found in a mother and her infant. Roentgenograms of the skulls of 22 other infants, however, showed no evidence of cranial calcification characteristic of toxoplasmosis.

DIFFERENTIAL DIAGNOSIS

The diagnosis of retrolental fibroplasia is usually not difficult to establish. Retinoblastoma and pseudoglioma are the two conditions with which it might easily be confused. Differentiation usually is not difficult in the other conditions which resemble it to any extent.

In retrolental fibroplasia there is commonly a history of premature birth with a weight at birth which is usually less than 4 pounds. The gross ocular signs and symptoms, which have ordinarily become evident by the third or fourth month, are poor vision, strabismus, nystagmus and microphthalmos. Close examination reveals the following signs, which are as a rule bilateral: (1) lack of differentiation of the iris; (2) shallow or flat anterior chamber; (3) presence of posterior synechias; (4) presence of a membrane behind the lens; (5) elongated

processes of the ciliary body; (6) vessels radiating over the surface of the membrane from a central point, and (7) presence of retinal detachments, folds or other retinal anomalies, which may be seen if the membrane is not complete and does not, therefore, cover the entire retrolental space.

Retinoblastoma, which usually manifests itself later than retrolental fibroplasia, is seen in an eye of normal size and appearance which apparently has previously had good vision. At the outset the involvement in retinoblastoma is usually unilateral. A grayish or yellowish white nodular mass, with a glistening surface, may be observed in the fundus. Many tortuous, newly formed vessels spread over the surface, and hemorrhages and grayish foci of degeneration are frequently seen. In the majority of cases of retinoblastoma roentgenographic examination of the eye reveals the presence of granular deposits of calcium in the tumor.

Pseudoglioma is usually unilateral and generally follows one of the acute infectious diseases, especially meningitis. It is likely to be associated with more pain and congestion than is seen in early retinoblastoma or retrolental fibroplasia. It may further be differentiated by the lack of roentgenographic evidence of calcium deposits and failure of progression of the process.

Tuberculous or syphilitic granulomas and Coats's disease (retinitis exudativa) should be more easily differentiated.

CONGENITAL ANOMALIES

Congenital anomalies were not strikingly evident in our series of cases. The only one to occur in significant numbers was cutaneous hemangioma. Reese and Payne,[9] who were the first to note the relation of hemangioma to retrolental fibroplasia, found that 20 per cent of their patients had hemangiomas of the skin at birth. Krause,[10] in discussing congenital anomalies, stated that hemangiomas of the occiput and chest were found in his cases. Kinsey and Zacharias [6] reported that the incidence of hemangiomas in premature infants with retrolental fibroplasia was 14 per cent but pointed out that the incidence for premature babies with unaffected eyes is 15 per cent.

In our total series of 238 patients, hemangiomas of the skin were present in 40 patients (17.5 per cent)—28 males and 12 females. They were not found in any of the 10 full term infants; thus the incidence did not differ significantly from that reported for premature infants in this area who did not exhibit retrolental fibroplasia. It is interesting in this connection that Hess, Mohr and Bartelme [11] gave the normal incidence of hemangiomas of the skin for full term infants as 0.5 per cent, and for premature infants as 3.2 per cent.

COMPLICATIONS

Synechias were the commonest complication found in our group. Posterior synechias are of two types. In the first type, long, strandlike bands extend from the anterior surface of the iris to the anterior capsule of the lens. They apparently extend along the tracks of previous branches of the pupillary portion of the tunica vasculosa lentis. The pupillary membranes, which are seen in newly born infants, have usually almost completely disappeared by the time retrolental fibroplasia has developed. The second type is composed of the usual adhesions between the posterior surface of the iris and the lens and resembles the adhesions ordinarily formed in iritis. In retrolental fibroplasia, however, they occur in the absence of iritis. They probably arise from irritation caused by mechanical pressure exerted by the lens, which is displaced forward against the iris. In some patients the pupil may be bound down firmly to the lens. Iris bombée was rarely found in the present series. This, with the adhesions between the iris and the lens, is evidence of faulty formation of aqueous humor.

Anterior synechias may form in cases of longer standing as the anterior chamber continues to flatten. In such cases the lens or the iris, or both, may be brought into contact with the posterior surface of the cornea. Areas of atrophy of the iris, as well as corneal opacities, frequently develop at the site of these anterior synechias. As a rule, anterior synechias form much later than posterior synechias. Posterior synechias were found in 64 per cent of our patients, whereas anterior adhesions were present in only 15 per cent. These percentages will obviously increase, however, with the age of the children.

Glaucoma is an important complication in retrolental fibroplasia. It was detected in 43, or 16 per cent, of our patients. Both eyes were involved in 13 of the patients. In all but 5 the glaucoma developed at some time after the completion of the fibroplasia, when the anterior chamber had become extremely shallow or flat and after formation of synechias was extensive. Five of the patients had buphthalmos, which in 2 involved only one eye. These 5 patients were found to have glaucoma at the time of their first visit to us, so that we are unable to determine the time of onset of the glaucoma. The disease, did, however, manifest itself before the usual time of appearance of secondary glaucoma in the remaining patients.

Secondary glaucoma in retrolental fibroplasia can usually be controlled surgically or by the use of miotics; in some instances, the tension subsides of its own accord. Nevertheless, vision was ultimately destroyed or reduced to bare perception of light in all our cases. It should be borne in mind that glaucoma develops in the eyes with membrane and synechia formation, retinal detachment and, in some cases, late hemorrhages. It is obvious, therefore, that, in spite of the possi-

bility of controlling the increased tension, there is little or no chance of saving vision in an eye in which secondary glaucoma develops. The ultimate fate in some of the glaucomatous eyes in our group has been phthisis bulbi. Fortunately, except in the rare acute case, the glaucoma is usually relatively asymptomatic. It is also fortunate, for the comfort of the patient, that the tension does not usually remain elevated indefinitely, even when therapeutic measures are unsuccessful in reducing it. This eventual decrease in intraocular tension is probably due to maldevelopment or atrophy of the ciliary body, with resulting lack of aqueous formation. Fifteen of our patients were operated on for glaucoma, usually with control of the tension, but with ultimate blindness in each case. Because of the inability to save vision, we have, therefore, resorted of late to surgical procedures in only the few cases in which severe, painful glaucoma has developed. We have not felt justified in operating in the milder, relatively asymptomatic, cases. Enucleation for painful glaucoma has been necessary in only 4 of our cases.

The importance of retinal complications in retrolental fibroplasia cannot be overemphasized. Terry [4] stated:

> Various disturbances of the retina may be seen, such as retinal separation (usually in the form of a long, narrow, whitish ridge which follows the general course of the blood vessels), retinal folds, or a healed lesion of chorioretinitis.

Owens and Owens [5] stated:

> In these infants the initially normal fundus picture was replaced by an angiomatous dilatation of the retinal vessels, followed by massive retinal exudation, retinal detachment, and the formation of a retrolental membrane.

They found that in all their cases the retrolental membrane appeared to result from the extension across the retrolental space of fusing peripheral detachments of swollen, grayish retina. Krause,[10] in summarizing the pathologic features of 16 eyes which he had removed, found that 7 of the 9 microphthalmic eyes had a totally detached retina. He also found that the eye of a full term infant with microphthalmos had a long-standing retinal detachment and retinal synechias at birth. He stated:

> Two of the 9 microphthalmic eyes had no retinal detachment. One showed general retinal dysplasia, and the other, general retinal gliosis, atrophy and glial hyperplasia of the anterior part of the retina and persistent hyaloid artery.

Reese, in discussing the Owenses' [5] paper, stated:

> It is my feeling, therefore, that in all cases of retrolental fibroplasia at least the matrix of the lesion is present at birth and consists of hemangiomatous-like tissues around the base of the vitreous with accompanying hemorrhage, organization and detachment of the retina.

In our series it was impossible to visualize the fundus of many of the patients. One hundred and twenty-eight of them had a complete retrolental membrane, in some cases further complicated by cataract,

opaque cornea or blocked pupil. In 110 of the patients, however, in one eye at least, the membrane was incomplete, so that portions of the fundi could be observed. In 82 of these 110 patients whose fundi could be seen, retinal detachments and folds were found. Likewise, with few exceptions, degenerative changes in the retina were observed, with or without retinal detachment.

In spite of the presence of retinal folds and detachments, 30 of our group of patients have thus far retained some vision. Eyes with folds and detachments rarely have good central vision. A child, aged 4 years, with folds and a detachment in each eye has a visual acuity nevertheless of 20/30 in each eye. The retrolental membrane is limited in extent to the outer lower quadrant in each eye. The child was born eight weeks prematurely and weighed 3 pounds 4 ounces (1,474 Gm.). Another child, one of twins, born six weeks prematurely and weighing 3 pounds 8 ounces (1,588 Gm.), who has partial membranes with retinal detachments in each eye at the age of 7½ years, still has a visual acuity of 20/200 in each eye. Twenty-eight children are able to recognize small objects but have acuities, as well as can be determined, of less than 20/200. It is, of course, questionable how long vision will be retained in such eyes with retinal folds and detachments. Two of our patients who had retained 20/200 vision for over five years suddenly became completely blind from total retinal detachments.

That ocular hemorrhages may occur in the early developmental stage of retrolental fibroplasia is an established fact. The Owenses,[5] in observing the early development of the disease, found that occasionally small hemorrhages occurred into the membrane from radiating vessels in the membrane. Our data show that the hemorrhages may still be present for months after the membrane has been completely developed and that occasionally new hemorrhages may occur in the late stages of the disease. Hemorrhages were observed in 22, or 9.6 per cent, of the 238 patients in our group—21 premature and 1 full term infant. In 15 patients they were present at the time of our first examination; they probably remained as residual hemorrhages from the early developmental period of the disease. In 7 of our patients new hemorrhages occurred after the age of 2 years. The hemorrhages were found on the membrane in 17 eyes; in the vitreous in 3 eyes, in the retina in 2 eyes and in the anterior chamber, occurring at the age of 2 years, in 1 eye.

MENTAL RETARDATION

Blind children in general, as compared with sighted children of the same age, are retarded; but this retardation is usually only apparent. The behavior patterns common to blind children are present in retrolental fibroplasia. Because of these "blindisms," such as rocking, swaying, headbanging, twitching, screaming and teeth grinding, in

common with slower motor development, many children with retrolental fibroplasia have been given a diagnosis of mental retardation. Prematurely born children in general are slower in developing than full term children. According to Hess, Mohr and Bartelme,[13] mental retardation occurs in about 10 per cent of all premature infants. There is as yet no test to determine the intelligence of the preschool blind child.

Twenty-six of the children in our group have reached the school age; 23 are now attending school—13 at the Perkins Institution—and of this number the mental development of 9 had been diagnosed as retarded. The scholastic records of these 9 children show that their intelligence is average or above average.

At present studies are under way by the pediatrics and child psychiatry groups at the Massachusetts General Hospital to determine what should be expected of the child who is born blind in terms of his physical, mental and emotional development. Thus far it does not seem that children with retrolental fibroplasia show any higher incidence of real retardation than the average group of premature children. At present it does not seem feasible to make a diagnosis of retardation without full evaluation of the "emotional climate." These studies on what should be expected of a child with retrolental fibroplasia will be published early in the fall.

VISUAL ACUITY

The visual acuities in a group of children whose ages range from a few months to 8 years are necessarily difficult to determine accurately. Such a large series of patients, with so much individual variation of acuity, makes a final tabulation of the vision difficult. Even after the tabulation, one has none too accurate a gage, since the vision does not remain constant in these patients. In a very large majority the vision decreases with time, whereas in a very small minority improvement occurs.

For the sake of convenience, we have attempted to classify the visual acuities under the following five headings: (1) no vision; (2) ability to see light and shadows; (3) ability to see objects of various sizes; (4) vision of 20/200 and (5) vision better than 20/200 in at least one eye, or, in the younger children whose acuity it is impossible to determine, what we consider to be good vision.

The visual acuities of the 210 children on whom we are able to report are as follows:

Group 1:	No vision	71 patients
Group 2:	Ability to see light and to detect hand movements	70 patients
Group 3:	Ability to see and reach for objects of various sizes	46 patients
Group 4:	20/200 vision in the better eye	6 patients
Group 5:	Vision better than 20/200 in the better eye	17 patients

Five of the patients in group 5 have been found to have an acuity in the better eye of 20/30; 2, of 20/40, and 2, of 20/60. Eight of the patients in group 5 are too young to have their acuity determined; it is evident, however, that they have good vision in the better eye. Our data indicate that full term infants have a better chance of acquiring serviceable vision than do prematurely born infants. This is suggested by the observation that 5 of our 10 full term infants have better than 20/200 vision, whereas only 12 of 200 premature infants have 20/200 vision or better. It should be recalled that the macula normally does not differentiate completely until six months after birth at full term. The searching nystagmus, which is almost invariably present in early retrolental fibroplasia, is undoubtedly indicative of a poorly developed macula. It seems, therefore, that an abnormality such as retrolental fibroplasia, which occurs before the macular region is differentiated, would prevent its differentiation, with resulting poor visual acuity.

TREATMENT

Since the prognosis in retrolental fibroplasia is unfavorable, medical and surgical therapy are of questionable value. An attempt should be made, however, to prevent complications, such as the formation of synechias and the development of glaucoma, as well as to treat glaucoma if it develops.

It has been our custom to use a mydriatic in an attempt to prevent the formation of synechias or, if possible, to break synechias which have already formed. Since glaucoma is a not infrequent complication of retrolental fibroplasia, caution must be exercised in the use of any mydriatic. To produce mydriasis, we have used a solution containing a combination of 1 per cent homatropine hydrobromide and 1 per cent paredrine® hydrobromide ophthalmic,[14] the action of which is powerful but of short duration. To lessen the possibility of producing glaucoma, we have used a solution of 1 per cent pilocarpine nitrate several hours after the instillation of the mydriatic.

Our routine, up to the age of 1 or 2 years, has been to use the mydriatic one or two mornings a week and then the miotic in the evening of the same day. In many cases there is a marked tendency toward formation of synechias with no tendency to the development of glaucoma. In such patients we have frequently resorted to the daily use of the mydriatic and have discontinued the use of miotic. The routine use of pilocarpine alone seems to have been beneficial in some cases of glaucoma.

14. Paredrine® hydrobromide ophthalmic is a 1 per cent solution of para-hydroxy-α-methylphenylethylamine hydrobromide in distilled water, made tear isotonic with 2 per cent boric acid and preserved in merthiolate (1: 50,000).

In the older infants, if the anterior chamber tends to deepen and there is evidence of growth of the eye, there is little danger of synechia formation or the development of glaucoma. Medication has been routinely discontinued in such cases, as well as in the older patients whose eyes have shrunken and become totally blind.

Surgical measures, in our hands, have been disappointing. The elevated tension in glaucoma which fails to respond to medication may be controlled by various forms of glaucoma surgery; nevertheless, the ultimate result is usually blindness. Blind eyes which are painful should, of course, be enucleated. It is conceivable that surgical intervention might be beneficial in certain cases of retrolental fibroplasia which occur, especially in full term infants. The lenticular-patellar type, for instance, might be benefited by the removal of the crystalline lens.

Radiation therapy was used unsuccessfully by Terry in 2 of our cases; our experience with this form of therapy, however, has been too limited to permit its evaluation.

A most important and valuable form of therapy has been rendered through the social service department and the psychiatric department and by our nursery school teacher.

It is clear that therapy for retrolental fibroplasia is, at present, not encouraging. Hope must therefore be placed in a knowledge of its etiology and in its prevention.

CONCLUSIONS

The cause of retrolental fibroplasia is unknown. Prematurity and weight at birth are predisposing factors in a large majority of cases. Two hundred and twenty-eight of our patients were born prematurely, 60 per cent of whom were born from eight to eleven weeks before term. All of the premature infants weighed less than 5 pounds at birth, 85 per cent weighing less than 4 pounds.

Multiple births occurred 54 times in our series. This is apparently significant only with regard to the relation of multiple births to prematurity.

Maternal disease during pregnancy had no bearing on the occurrence of retrolental fibroplasia in the infants.

Congenital anomalies were not strikingly evident in our series. Hemangiomas of the skin occurred in 17 per cent of the premature infants. This incidence is only slightly higher than the 15 per cent incidence found by Kinsey and Zacharias[6] in premature infants who did not have retrolental fibroplasia.

The common complications of retrolental fibroplasia were synechias, secondary glaucoma, retinal detachments and cataract.

Psychiatric studies on our group thus far do not indicate that there is a higher incidence of real mental retardation than is found in the average group of prematurely born children.

Seventy-one children were totally blind; 21 of 210 children, whose vision could be determined, had vision of 20/200 or better in at least one eye.

Treatment of retrolental fibroplasia is purely symptomatic. There is at present no cure for the disease.

ABSTRACT OF DISCUSSION

DR. WILLIAM OWENS, Baltimore: Dr. King's observations were made on infants who were at least 6 months of age when first examined. Our experience with the late stages of this disease is essentially the same as Dr. King's. In the late stages there is little that can be done. We agree that the results of surgery were very poor. In our experience, if secondary glaucoma occurred, it always subsided with the use of miotics alone, and surgical intervention was not necessary. Before our observations on the early course of the disease showed that the abnormality was primarily a disease of the retina, we operated in an attempt to remove the retrolental membrane. In every case the membrane removed was found to contain disorganized retina when examined histologically; so this operative procedure was abandoned.

During the past four years we have seen retrolental fibroplasia develop in 50 eyes of 25 infants. In every case the eyes showed no abnormality at birth. All remnants of the hyaloid artery had disappeared before the onset of the early stage of the disease. The earliest detectable abnormality was dilatation of the retinal vessels, followed by extensive retinal edema. The arteries became tortuous, resembling corkscrews or ribbon candy. The retinal vessels became partially buried in masses of swollen retina. As the disease progressed, the vitreous became hazy and the swollen retina raised. In most cases the peripheral folds of retina fused behind the lens to form a complete membrane. In some the disease was arrested before a complete membrane was formed, and in these cases a great variety of end pictures resulted.

The changes seen in the anterior segment of the eye in the advanced stages, such as the small cornea and the shallow anterior chamber, were the late results of the arrest in growth of the eye. In none of the eyes in which retrolental fibroplasia developed was the cornea smaller than normal, or the anterior chamber abnormally shallow, before the onset of the disease in the retina. Occasionally megalocornea resulted in the late stages, but in our experience it occurred only in association with glaucoma. Retinal folds, myopia and extensive areas of retinal atrophy with scarring and pigmentation were frequently seen as an end result of the disease.

These observations indicated that the disease was not of congenital origin, and that it was not related to persistence of the hyaloid artery. We concluded that the disease was metabolic in origin. We have recently been investigating the relation of the disease of a possible vitamin E deficiency. For the past year, one-half the infants with birth

weights of 3 pounds or less in the premature Infants Nursery of the Harriet Lane Home of the Johns Hopkins Hospital have been receiving vitamin E supplements. The other half with similar birth weights have received no vitamin E supplement. In the group that received vitamin E supplements, no cases of retrolental fibroplasia have occurred, while in the group not given the supplement the disease has occurred with the usual incidence for this nursery, that of 15 per cent.

DR. ARTHUR C. UNSWORTH, Hartford, Conn.: Dr. King has undoubtedly seen more cases of retrolental fibroplasia than any one else. He deserves the gratitude of the medical profession for his long follow-up study of these cases, his patient examinations and his careful recordings of his observations.

The Owenses have greatly advanced knowledge of the etiology and, we hope, prevention.

I have seen retinal vascular disease of metabolic origin in premature infants, some with dilated vessels, but in all it subsided before the development of retrolental fibroplasia.

In a great many patients the pathologic change is not sufficient to have been recognized as retrolental fibroplasia in early life. Later when the patient is seen by the ophthalmologist for strabismus or poor vision, the lesion observed may be diagnosed as a congenital abnormality—congenital retinal fold, septum frontale, retinal fibrosis, vitreous veils, vitreous cysts, persistence of the hyaloid artery, congenital high myopia, microphthalmos, toxoplasmosis or extrapapillary coloboma. On questioning the parents, the physician may learn that the baby was premature and was very small at birth. In at least some of these cases the condition is an arrested retrolental fibroplasia, which would have exhibited active signs if observed during the first few months of the infant's life.

Retrolental fibroplasia always has a tendency to regress; unfortunately, any appreciable degree of the disease apparently results in permanent damage to central visual acuity. The disease behaves like an inflammatory process. Therefore, atropinization should be used in treatment, at least during the active phase, when I feel that it is of definite benefit in preventing the complication of posterior synechias.

I should like to ask Dr. King what he usually finds as the refractive error in these children, and whether there is any correlation between the refractive error and the vision obtained. Has there been any regression in the cases after the age of 1 year?

DR. MERRILL J. KING, Boston: I should like to thank Dr. Owens for his discussion and compliment him on the beautiful work that he and his wife are doing at Johns Hopkins.

Dr. Unsworth suggests that in practice ophthalmologists should be on the alert, even in older children, to detect cases of this anomaly which have not been previously recognized. We have had several such patients, all of whom were born prematurely.

As to toxoplasmosis, we have found definite evidence of the disease in the infant and mother in 1 of our cases. Roentgenograms of the skulls of approximately 25 other infants revealed no evidence of toxoplasmosis.

Dr. Unsworth recommends the use of atropine because he considers the disease inflammatory. Those of you who know the early work of

Dr. Terry will recall that he, too, advised the use of a mydriatic, one that would act quickly and strongly, but would not have a lasting effect. He, however, recommended the use of a miotic several hours after the pupil had been dilated. Usually we have carried out his procedure. We use a solution consisting of equal parts of 1 per cent homatropine hydrobromide and 1 per cent paredrine® hydrobromide ophthalmic in the morning and in the evening of the same day a 1 per cent solution of pilocarpine nitrate. The purpose is to prevent the formation of synechias. After the age of 1 or 2 years, if activity seems to have subsided, we have discontinued the medication.

Dr. Owens stated that he did not often operate for the secondary glaucoma because in most instances the tension subsided of its own accord. That has also been our experience. The tension does go down usually, whether operation is or is not performed.

As to refractive errors, about 55 per cent of the children on whom we have been able to do refractions are myopic.

I should like to pay a tribute to Dr. Terry, who started the work on retrolental fibroplasia and accomplished so much. During the last eight or nine months of his illness, I helped him, and I have tried to carry on since his death.

USES OF NAPHAZOLINE (PRIVINE®) IN OPHTHALMOLOGY

PAUL HURWITZ, M.D.
CHICAGO
AND
JOHN M. THOMPSON, M.D.
SOUTH BEND, IND.

NAPHAZOLINE hydrochloride (privine®; 2-[1-naphthyl-methyl]-imidazoline hydrochloride) has long been in use as a nasal decongestant. Heretofore, however, it has not been used in ophthalmology in this country. Since its properties indicate potential usefulness as an ocular decongestant, it was decided to determine its value in a number of clinical conditions. It became evident that naphazoline hydrochloride in ophthalmic solution could be a valuable adjunct to the ophthalmologic armamentarium. Hence a series of experiments was conducted to determine the effect of naphazoline on intraocular tension, pupillary size, accommodation and status of the ocular blood vessels.

Naphazoline hydrochloride [1] in 0.1 per cent ophthalmic solution has the following formula:

Naphazoline hydrochloride	0.1 Gm.
Boric acid powder	4.0 Gm.
Sodium borate U. S. P.	4.5 Gm.
Camphor water U. S. P.	20.0 cc.
Distilled water q. s.	100.0 cc.

CLINICAL APPLICATION

Babel [2] and Fanta [3] reported on the effect of naphazoline on the eyes of rabbits and human subjects. In view of the contemplated manufacture of privine® ophthalmic solution for the commercial market, it was deemed advisable to publish the results of our experimental work, covering more than 100 patients. The solution was found to have considerable sustained decongestant effect in cases of hyperemia of the palpebral and bulbar conjunctivas and in cases of superficial corneal vascularity from all causes. Naphazoline also favorably influenced the

The experimental phase of this work was done at the University of Illinois, Department of Ophthalmology (Illinois Eye and Ear Infirmary), Chicago.

1. Ciba Pharmaceutical Co., Summit, N. J., supplied the privine® and facilitated this work by a special grant.

2. Babel, J.: Schweiz med. Wchnschr. **71**:561 (April 26) 1941.

symptoms of photophobia, lacrimation, blepharospasm, itching and burning, occurring in many ocular diseases, of various causes.

Included in this series were cases of chronic catarrhal conjunctivitis, allergic conjunctivitis, vernal conjunctivitis, keratitis (secondary to syphilis and of other types) and corneal pannus. There were also cases of bulbar congestion due to chemical burns, trauma, chronic iridocyclitis, endophthalmitis and postoperative states. A number of such cases are now briefly described.

CASE 1.—*Postoperative (cataract extraction) complications of uveitis and keratitis.*

Intense bulbar injection was present, as well as superficial and deep corneal vascularity. The symptoms consisted of severe photophobia and ocular discomfort, dating from the time of operation, four months before. Naphazoline hydrochloride, 0.1 per cent solution, instilled four times daily, resulted in rapid ocular ischemia and almost immediate amelioration of the symptoms. The continued use of the solution gave sustained relief.

CASE 2.—*Recurrent attacks of rosacea keratitis for several years.*

Superficial corneal opacities and numerous superficial vessels were evident. Two previous attacks, while the patient was under treatment, had persisted eight months and four months, respectively. In the third attack several months later, treatment was supplemented with the naphazoline solution. Improvement resulted in ten days. Significant was the marked decrease in the conjunctival and corneal vascularity and the reduced photophobia and blepharospasm.

CASE 3.—*Diffuse phlyctenular keratitis with profuse lacrimation and intense photophobia.*

The patient had worn smoked glasses day and night for many months. The instillation of naphazoline immediately allayed the photophobia and lacrimation and effected rapid improvement.

CASES 4 and 5.—*Syphilitic interstitial keratitis.*

Both patients had distressing photophobia, which was dramatically relieved with 0.1 per cent naphazoline hydrochloride solution instilled three times a day.

CASE 6.—*Bilateral chronic squamous blepharoconjunctivitis and photophobia.*

Though the pathologic process did not yield to any of many forms of therapy, the photophobia was relieved by the use of naphazoline solution.

CASE 7.—*Epiphora of the right eye.*

No objective pathologic condition was found. The use of naphazoline relieved the epiphora.

CASE 8.—*Chemical burn of the conjunctival sac and cornea of both eyes.*

The sequelae consisted of mild symblepharon and intense conjunctival and corneal vascularity, with severe photophobia and blepharospasm. Naphazoline reduced the vascularity, photophobia and blepharospasm and permitted an early return of the patient to his occupation as truck driver.

CASE 9.—*Vernal conjunctivitis with distressing photophobia.*

Antistine® solution (2-[N-phenyl-N-benzylaminomethyl]-imidazoline) afforded substantial symptomatic relief. The addition of naphazoline to the treatment further improved the tolerance to light.

CASE 10.—*Vernal conjunctivitis.*

Naphazoline solution reduced the photophobia.

In many cases of chronic catarrhal conjunctivitis (perhaps more properly classified as congestive states of the conjunctiva), associated with symptoms of tearing, burning and redness of the eyes, naphazoline solution was used. In the majority favorable symptomatic responses, of varying degrees, occurred. In many cases of allergic conjunctivitis, naphazoline solution was found to decrease the photophobia and tearing. In cases of epiphora due to catarrhal inflammation of the mucous membranes of the lacrimal system, and with intermittent obstruction to lacrimal drainage, naphazoline solution occasionally proved of aid. In such cases decongestion of the canaliculus and the wall of the sac facilitated the flow of tears and mucoid discharge.

Naphazoline had definite value in surgical procedures, in the presence of ocular congestion or capillary bleeding. Its strong vasconstrictor action (and the absence of secondary vasodilatation) made it a satisfactory topical hemostyptic agent.

Naphazoline in 0.1 per cent solution was well tolerated by the eye. Mild to moderate burning was experienced on instillation. Occasionally, the drug produced an annoying itching. Several patients with lightly pigmented irises complained of sporadic blurring of vision. Over prolonged periods of use, up to nine months, no irritating or untoward effects were noted. The sequela, described after prolonged nasal use, of vascular engorgement secondary to capillary contractile paralysis, was not observed in ocular use.

EXPERIMENTAL RESULTS

Intraocular Tension.—In 60 patients (120 eyes), with intraocular tension ranging from 14 to 34 mm. of mercury (Schiötz), 3 drops of 0.1 per cent naphazoline hydrochloride solution were instilled, the instillations being made at five minute intervals. The tension was taken one hour later. With an acceptance of 2 mm. of mercury as a normal variation in

TABLE 1.—*Distribution of Increased Intraocular Tension with Instillation of Naphazoline Hydrochloride in 20 Eyes*

No. of Eyes with Increased Tension	Increase in Tension, Mm. Mercury
9	2.00
6	4.00
3	5.00
1	6.00
1	7.00

successive tonometric readings, it was noted that only 25 eyes showed any abnormal variation in tension. Twenty eyes showed an increase and 5 eyes a decrease in tension. The 20 eyes with increased tension in table 1 are classified according to the amount of increase. These eyes represent 15 patients, 13 of whom had lightly pigmented irises.

These eyes are classified again in table 2 with tonometric readings, before and after the instillation of naphazoline hydrochloride.

In the eyes with tensions ranging from 30 to 34 mm. of mercury, no increases in intraocular pressure followed the instillation of naphazoline hydrochloride, 0.1 per cent solution. In no case was glaucoma precipitated or aggravated.

Of the 5 eyes in which tension was decreased, the pressure decreased 3.0 mm. in 2, 4.0 mm. in 2 and 5.0 mm. in 1 eye.

TABLE 2.—*Tonometric Readings in 20 Eyes Before and After Instillation of 0.1 Per Cent Naphazoline Hydrochloride*

Intraocular Tension, Mm. Mercury			
Before	After	Before	After
15	22	24	28
16	20	24	30
16	21	25*	28
19	22	25	29
20	23	26	29
21	24	26	30
22	26	28	31
23	27	29	32
24*	27	29	32

* Two eyes.

TABLE 3.—*Effect of 0.1 Per Cent Naphazoline Hydrochloride on: Pupillary Size in 120 Eyes*

Status of Pupil	No. of Eyes	Change in Pupillary Size		
		1.0 Mm.	2.0 Mm.	3.0 Mm.
No change	46	0	0	0
Increase	68	50	98	12
Decrease	6	6	0	0
Total	120			

Pupillary Size.—The effect of 0.1 per cent solution of naphazoline hydrochloride on the pupillary size was observed in these 120 eyes. The changes are represented in table 3. In 68 eyes the pupillary size increased. Of these eyes, 48 had lightly pigmented irises, and 20 had brown irises. Of the 20 with darkly pigmented irises, the pupillary size increased 1.0 mm. in 16 and 2.0 mm. in 4. The brown iris is thus noted as relatively unresponsive to the mydriatic effect of naphazoline hydrochloride in 0.1 per cent solution. The mydriatic effect on blue and gray irises begins a few minutes after instillation and lasts two to three hours or more. Despite a mydriatic effect of 3.0 mm., the pupillary response to light was only slightly influenced.

Amplitude of Accommodation.—The amplitude of accommodation in 28 patients, after the instillation of 0.1 per cent solution of naphazoline hydrochloride, evidenced no essential change. This group was repre-

sented by persons of various ages and included those with gray and those with brown irises. The effect of 0.1 per cent naphazoline hydrochloride on accommodation can be considered negligible. Babel [2] found that with higher concentrations of the drug (0.5 per cent) the reduction in accommodation was not more than 0.5 to 0.75 D.

Effect on Blood Vessels of Conjunctiva and Cornea.—Naphazoline had a pronounced ischemic effect on the bulbar and palpebral conjunctivas, as well as on the superficial corneal vessels. In most cases of superficial ocular hyperemia, from various causes, naphazoline was found to have an immediate and prolonged decongestant effect. This ischemia commenced immediately on instillation of the drug and lasted several hours.

Examination with the biomicroscope revealed contraction of the capillaries of the bulbar and the palpebral conjunctiva. In cases of superficial corneal pannus, naphazoline produced a marked and prolonged contraction of the corneal vessels. In these cases no secondary engorgement was evident. However, naphazoline had no effect on the deeper vessels. There was no noticeable contraction of the vessels in scleritis and episcleritis. The deeper corneal vessels of interstitial keratitis were likewise unaffected.

SUMMARY AND CONCLUSIONS

Naphazoline hydrochloride, in 0.1 per cent ophthalmic solution, was found to have a prolonged decongestant effect on the superficial cornea and the palpebral and the bulbar conjunctiva. It reduced ocular hyperemia in cases of chronic catarrhal, allergic and vernal conjunctivitis, keratitis due to any of many causes, chronic iridocyclitis and postoperative states. This response was facilitated by the rapid and striking contraction of the superficial conjunctival and corneal capillaries.

Naphazoline also reduced the symptoms of lacrimation, blepharospasm, burning and ocular discomfort associated with the aforenoted conditions. Most striking was the salutary reduction of photophobia.

The prolonged ischemia (without secondary vasodilatation) produced by naphazoline hydrochloride solution was valuable in interrupting the irritative phenomenon that frequently follows ocular infection and ocular surgery. This irritative cycle consists of hyperemia with resultant aggravated symptoms of congestion, thereby further increasing the hyperemia. Decongestion with naphazoline materially reduced the symptoms and thus favorably affected the congestive sequelae of disease processes.

The beneficial influence of naphazoline on lacrimal drainage was observed in certain cases of catarrhal inflammation of the lacrimal system with dacryostenosis and epiphora. It was also of value in cases of ocular

congestion, so-called chronic conjunctivitis, in which no evidence of infection was demonstrable. This condition is usually associated with photophobia, burning and a sensation of heaviness.

The prolonged vasoconstriction effected by naphazoline also makes it an ideal agent for topical hemostyptic purposes in ocular surgery.

The safety of naphazoline hydrochloride in 0.1 per cent solution, as an ocular decongestant, is demonstrated by the fact that only a small percentage of 120 eyes showed any significant increase in ocular tension. In none of the eyes with an intraocular tension above 30 mm. of mercury (Schiøtz) was the tension increased. The mydriatic effect of 0.1 per cent naphazoline hydrochloride is very mild and is limited almost entirely to lightly pigmented irises. The pupillary response is not materially altered, and the effect of naphazoline on accommodation is negligible.

Naphazoline is well tolerated, and even after prolonged periods its use has not resulted in irritative or toxic sequelae.

Naphazoline hydrochloride (privine® hydrochloride) ophthalmic solution, in 0.1 per cent strength, is advocated for use in conditions in which ocular decongestion is desirable.

55 East Washington Street, Chicago (2).

PHOTOGRAPHY OF THE RED REFLEX

VIRGINIA LUBKIN, M.D.
NEW YORK

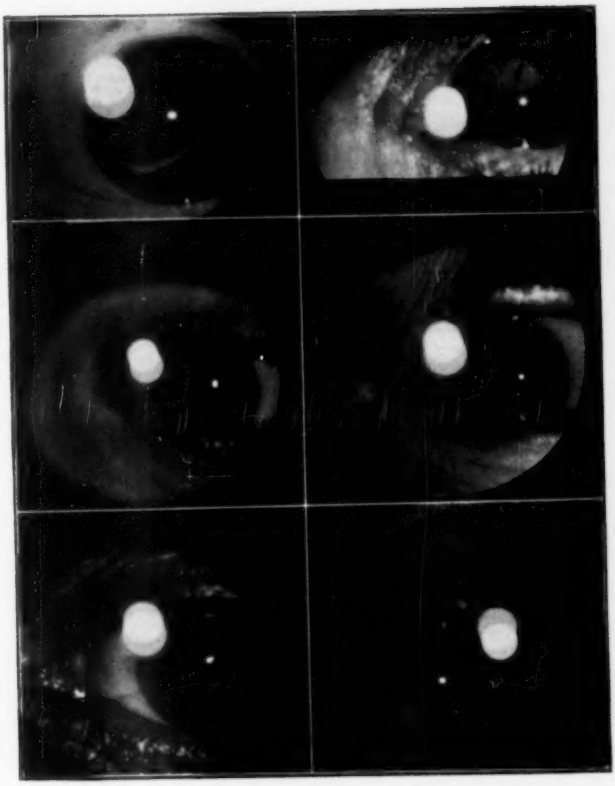
FROM time to time the exigencies of the private practice of medicine present one with fortunate problems the solution of which leads to new developments. In a case in point, that of an intraocular foreign body, it became a medicolegal necessity to demonstrate whether or not the associated traumatic cataract was progressive. It was obvious that depiction by a medical artist might be suspect and could at best not be completely objective, to say nothing of the cost. A photographic method was indicated, but none satisfactory was available.

After some thought, it seemed feasible to use the Nordensen fundus camera to photograph the cataract as viewed ophthalmoscopically by transillumination—in other words, to photograph the red reflex. Brief experimentation produced some remarkable results.

A review of the literature[1] on the use of the fundus camera showed no evidence of previous description of this surprisingly simple method. The technic consists in setting the camera up as usual, but in focusing it in the plane of the lens, or at whatever plane in the vitreous the lesion is located, instead of on the retina. For this purpose the chin rest is racked back a short distance farther than usual and a plus lens is used in the camera. The transilluminated silhouette is seen exactly as it appears when viewed with the ophthalmoscope through the plus 6.00 D. lens held about 1 foot (30 cm.) from the eye. With skilful handling, most of the dilated pupil is illuminated in the final picture, but commonly a dark crescent occupying one fifth to one fourth of the pupillary area is unavoidable. Therefore, it is important to be sure that the pathologic shadow which is being recorded is not caught in the dark patch. Particularly good effects are obtained when the optic disk is centered behind the pupil; the yellow-white background sets off lenticular opacities more strikingly.

The method is in general suitable for any lesion in the lens area which allows the passage of enough light through or around it to provide contrast. Cortical, nuclear, cupuliform, congenital and traumatic opacities of the lens; subluxations and deformities of the lens; masses,

1. A preliminary report of this study was presented at a meeting of the New York Academy of Medicine, Section of Ophthalmology, in February 1949.



Ocular abnormalities revealed by photographs of the red reflex: top left, dislocated lens (clinic case, New York Eye and Ear Infirmary); top right, cortical spokes; center left, posterior lenticonus (courtesy of Dr. J. Levitt, Brooklyn); center right, nuclear sclerosis; bottom left, neoplasm of the cilary body (courtesy of Dr. Wendell Hughes, Hempstead, N. Y.); bottom right, posterior subcapsular cataract.

such as tumors of the ciliary body, which intrude on the pupil; congenital aniridia; anomalies of the iris, such as posterior synechias which cast shadows in the red reflex, and certain shadows in the anterior portion of the vitreous, such as those caused by partial retrolenticular fibroplasia—all these will, by and large, appear in the photograph as they are seen with the ophthalmoscope.

This new photographic technic has many uses. There is the recording of medical curiosities. There is objective depiction for medicolegal cases with accuracy over a period of time, without the necessity of depending on memory or crude drawings. There is, too, a tool suitable for research—for example, in appraising the experimental treatment of cataract, or perhaps in following the stages of development and resolution of induced cataract. Finally, the new method creates a teaching device not hitherto in existence—a complete series for the undergraduate or graduate student of what one might label anomalies of the red reflex. A library of such pathologic findings is now available, as clinical cases are not, for detailed study at all times.

Mrs. M. Markham and Mrs. E. Brown, of the Department of Photography of the New York Eye and Ear Infirmary, and Dr. Wendell Hughes, its director, gave technical assistance in the development of the method.

128 East Seventy-First Street (21).

GLAUCOMA AT THE WILLS HOSPITAL

LOUIS LEHRFELD, M.D., F.I.C.S.
Attending Surgeon, Wills Hospital
AND
OWEN BELMONT, M.D.
Clinical Assistant, Wills Hospital
PHILADELPHIA

THE OPHTHALMOLOGIST, like the physician in other fields of medicine, has frequently a preconceived idea about the treatment of disease based on his personal experience and the experience of others recorded in the medical journals and textbooks. This is particularly true in the case of glaucoma. These fixed ideas become malleable under the influence of statistical research.

It was with the purpose of finding out the results of the present methods of handling glaucoma that we at the Wills Hospital sought to obtain the desired information by a survey, the result of which was published in the ARCHIVES.[1] This study covered a ten year period, from 1926 to 1935, and included the records of 1,876 patients, representing 0.78 per cent of a total of 242,533 patients admitted to the hospital for various reasons during that decade. Statistics from this survey were widely quoted by Duke-Elder in his section on glaucoma.

The aims and purposes of the first survey, however, were not fully realized. It is apparent that it is impossible to have a complete and accurate record of all patients at any one time. One must be satisfied with a statistical record of a smaller number of patients who are under constant care and for whom the ultimate outcome can be ascertained.

PRESENT SURVEY

For that reason, in this, the second, survey much of the incompleteness of the first is eliminated by an intensive study of records over a shorter period, from 1942 to 1947. The material is limited to 638 patients whose records were on file at the Wills hospital during those years and who were under observation for more than one year. All had had glaucoma for which some had been under observation for many years, the longest period being twenty-two years. No patient is included in the survey who was operated on elsewhere. The reason for such omission is self evident; no initial visual acuity or fields of vision, or clearcut

1. Lehrfeld, L., and Reber, J.: Glaucoma at Wills Hospital, 1926-1935, Arch. Ophth. **18**:712 (Nov.) 1937.

history, had been recorded prior to the date of operation, so that it was impossible to evaluate the end results observed at the Wills Hospital.

In the first survey, it was pointed out that the noncongestive type of glaucoma, commonly referred to as chronic simple glaucoma, constituted 72 per cent of all types of glaucoma and that of the remaining 28 per cent of cases, which were of the congestive type, 12 per cent were of the acute and 16 per cent of the chronic form. It was shown that 784 eyes had seriously damaged vision, below 6/60, when the patients first presented themselves for hospital care. This outstanding fact prompted us to sound the warning for the early detection of glaucoma by the founding and development of glaucoma clinics throughout the country.

The first survey also indicated that the most popular surgical procedure for the congestive type of glaucoma was a basal iridectomy and that the operation of choice for chronic simple glaucoma was trephination. It was also pointed out that in many cases of chronic simple glaucoma surgical intervention was not indicated and that miotics were used exclusively in at least half of all the cases, without recourse to surgery. The survey also indicated that the acute types of glaucoma were commoner in the group of 50 to 60 years, whereas chronic simple glaucoma was more frequently seen in the older group, from 60 to 70.

The present survey is statistical and is an estimation of the resultant effects on the patient, rather than on the individual eyes. In many instances it is possible to maintain vision in one eye, thus giving the patient sufficient visual acuity for useful purposes. Heretofore, the results, based on data on individual eyes, did not give a proper perspective. The surgeon who was unsuccessful in controlling glaucoma in one eye usually became conservative and resorted to medical or deferred surgical treatment of the opposite eye. Our statistics indicate the usefulness of both the patient's eyes. When both eyes are blinded the result is evidently a failure, but when one eye remains useful the experience with the first eye often changes the course of treatment of the second, resulting in adequate vision for practical use.

SELECTION OF CASES IN THE RECENT SURVEY

Only cases of primary glaucoma were studied in this survey. All records were from the nine clinics at the Wills Hospital during the period of 1942 to 1947 inclusive. Visual acuity was rated as excellent vision, good vision, partial blindness and blindness, as follows: excellent vision, 6/5, 6/6, 6/9, 6/12; good vision, 6/15, 6/21, 6/30; partial blindness, 6/60, 3/60; blindness, less than 3/60.

It was impossible to make quantitative measurements of loss of field because of the many irregularities of field forms and scotomas. For statistical purposes, therefore, form fields taken at 1 meter, with a 5 mm. test object will in this study be designated as follows: (1) full; (2)

slightly contracted, over 20 degrees but not full; (3) moderately contracted, 10 to 20 degrees, and (4) severely contracted, 10 degrees or less. Irregular scotomas were evaluated according to the deterioration in the patient's visual efficiency.

BUPHTHALMOS

It is surprising that in an institution as large as Wills Hospital only 10 cases of buphthalmos are recorded. This number compares favorably with that for the ten year period from 1926 to 1935, in which 28 cases were reported. It is our opinion, based on these statistics, that buphthalmos is a rare disease.

In 4 of the 10 cases only one eye is involved. In 1 of these 4 cases the patient was observed for ten years. At the age of 17 the unaffected eye had normal vision; the involved eye had vision of 6/9 ten years ago and of 6/12 now. The tension in the buphthalmic eye was originally 56 mm.; at the time of preparation of this report, in February 1949, it was 25 mm., four years after a modified Herbert sclerotomy. In 2 other cases of unilateral buphthalmos, operations were performed on the affected eyes, the condition of the normal eyes remaining stationary after one year of observation. In the other case of unilateral buphthalmos, the affected eye was operated on when the patient was under the age of 1 year, with resulting total loss of vision after trephination. In the cases of bilateral buphthalmos, in all of which the patients were first seen under the age of 6, operations were performed on both eyes. In 2 of these cases one eye each was saved, with a vision of 6/30, and in a third case visual acuity was 6/60 in each eye. In no instance in which buphthalmos was treated medically or surgically did the patient recover visual acuity in a sufficient amount to warrant any statement concerning the successful management of this disease.

Not a single eye with buphthalmos has been restored to useful vision. Restoration to an acuity of 6/30 may be recorded as excellent from the patient's standpoint, but it is not to be regarded as a noteworthy achievement on the part of the ophthalmologist. The present and the previous survey indicate that buphthalmos is a rare disease, the treatment of which is not yet satisfactory.

ACUTE CONGESTIVE GLAUCOMA

A total of 86 patients and 94 eyes had acute congestive glaucoma. Nineteen patients with unilateral involvement were treated medically. Sixty-seven patients, with involvement of 75 eyes, were treated surgically. Of these, 8 had bilateral and 59 unilateral involvement.

Of the 19 patients with unilateral disease who were treated medically, with observation over periods of one to fourteen years, 15 had initial good or excellent vision, as compared with 14 patients with good or

excellent vision at the time of this survey. It should be noted that we are now comparing patients, and not individual eyes, it being borne in mind that the patient with unilateral glaucoma usually has some preventive treatment for the opposite eye. If the end result is the saving of one eye for useful purposes, it is indeed an achievement in the patient's record of progress.

Of the 75 eyes treated surgically for acute congestive glaucoma, 25 had initial vision which was good or excellent, and the end result for 34 eyes was excellent or good vision. Fifty eyes were partly blind or blind when first seen; for 41 eyes the final result was partial blindness or blindness. Using the patient as a basis of analysis, and assuming that the patient, and not the individual eye, has glaucoma, it is found that 57 patients initially had good or excellent vision on a bilateral basis and 61 had good or excellent terminal vision.

In a final analysis of 67 patients with glaucoma, 59 of whom had operation on one eye and 8 on two eyes, 57 had good or excellent terminal binocular vision. Of the total 75 eyes, not 1 had an initial tension of less than 36 mm., but 45 had a final tension of less than 25 mm. and 12 of less than 35 mm. The tension of acute glaucoma can be reduced successfully by surgical means. The usefulness of the restored vision is in direct proportion to the damage already done by the disease. Although an individual patient may have full restoration of vision from the statistical point of view all eyes having an initial vision of less than 6/60 have a lower power of recovery than those having initial vision of more than 6/60.

In a further analysis of 8 patients with bilateral glaucoma treated surgically, 6 had a final result of good or excellent vision. One was partly blind and 1 totally blind.

Operative Procedures.—Of the 75 eyes treated surgically for glaucoma, some of which had more than one operation, 54 had a basal iridectomy, 13 trephining and 7 iridencleisis. The remaining, miscellaneous procedures included sclerotomy, sclerectomy, iridotasis, cyclodialysis, a modified Lagrange operation, retrobulbar injection of alcohol (secondary operation), iridodialysis and iridectomy, and incidental cataract extraction (7 cases); enucleation was the final procedure in 11 eyes. The enucleation of 11 of 75 eyes with acute congestive glaucoma is not a measure of the efficacy of the treatment but, rather, a reflection on the patients, who reported too late for effective treatment.

CHRONIC CONGESTIVE GLAUCOMA

Thirty-one eyes were observed. Nineteen had unilateral involvement, and all were treated surgically.. Twelve had bilateral glaucoma; of these, 7 were treated surgically and 5 medically. It is interesting to note that 4 of the 5 medically treated eyes with bilateral glaucoma had

good or excellent final vision, although 4 of 5 were blind or partly blind at the beginning of treatment. This result is not to be interpreted as indicating that blind eyes ultimately have good vision. An eye with acute or chronic glaucoma and visual acuity of less than 3/60 may be restored to good vision.

Sixteen eyes had excellent or good initial vision; 15 were partly blind or blind. In the final records only 8 eyes had excellent or good vision, as compared with 23 which were partly blind or blind.

If the reduction of tension has a degree of merit, and all agree that it does, it may be noted that there were, at the onset, only 4 eyes in which the tension was under 35 mm. A final tension of 35 mm. or less was recorded in 26 eyes, and of these 23 had tension of less than 25 mm.

Operation for glaucoma was performed on 26 patients, or 31 eyes. For 24 of these patients the initial binocular vision was excellent or good; for 20 the final vision was excellent or good. The point of importance is the finding that not one of the 31 eyes operated on for chronic congestive glaucoma was enucleated. It should also be noted that the end results were good so far as the patient was concerned, it being kept in mind that the fellow eye was potentially glaucomatous. As a final note, chronic congestive glaucoma, which comprises the smallest group of glaucomas, carries a good prospect for visual recovery.

Trephining was performed on 19 eyes, basal iridectomy on 8, the modified Lagrange operation on 3 and the modified Herbert sclerotomy on 1.

CHRONIC SIMPLE GLAUCOMA

Three hundred patients were treated medically, and 180, surgically. Of the latter, 101 had operations on one eye and 79 on 2 eyes. Because of the large number of cases involved in this category, namely, 480, the estimation of visual efficiency of the patient using two eyes is the basis of grading.

Of the 300 medically treated patients, 89.4 per cent began treatment at the Wills Hospital with excellent or good initial vision in both eyes; 79 per cent of the same group had a final vision which was excellent or good; for 21 per cent the final result was partial blindness or blindness. In other words, 10 per cent of those who had initially good vision were transferred statistically into the group with poor vision. Although approximately 200 of these patients were observed for one to four years, 100 of them were observed from five to nineteen years. It was pointed out in the first survey that a large majority of patients with chronic simple glaucoma are in the age groups of 50 to 60 and 60 to 70, most of them being in the latter. If the sight of the better eye in a case of chronic simple glaucoma can be preserved so that the patient maintains sufficient vision for occupational or ordinary purposes, it is a gain worth while. A visual efficiency rated as good or excellent, which

was experienced as the initial bilateral vision by 89.4 per cent of patients with chronic simple glaucoma and as final vision by 79 per cent of the same group is not a very serious loss.

The very fact that 300 patients were treated medically is in itself an indication that there is a medical phase of the treatment of chronic simple glaucoma which must be reckoned with and which is acceptable and practical. It does not follow that all patients with chronic simple glaucoma may do well under medical care alone. It is pointed out that 180 of a total of 480 patients were treated surgically. Such treatment was performed on one or both eyes because of the loss of vision and the inability to control intraocular tension and the fields of vision.

Of the 180 patients receiving surgical treatment of one or both eyes, 91.7 per cent had excellent or good initial vision in the eye operated on, and 8.3 per cent were blind or partly blind in one eye. The final records indicate that 65 per cent had excellent or good vision and 35 per cent were partly blind or blind. It should be remembered that the indication for surgical intervention was threatened blindness. Therefore the surgically treated eyes were those with poorer prospects than those treated medically. The end result, showing a decrease from 91.7 to 65 per cent for good or excellent vision, does not in itself indicate that operation was responsible for this loss; rather, it means that the eyes operated on were already losing their battle against glaucoma. It is my personal experience, however, that older patients with chronic simple glaucoma have some loss of vision after surgical experience and that many others lose ground, even though the tension has been reduced to normal or subnormal.

It is a statistical fact that the 300 patients with chronic simple glaucoma treated medically did fairly well. Those with uncontrolled tension and loss of vision did not do so well as a group treated surgically. Without surgical treatment they may have fared still worse. Statistics and experience are still not sufficiently extensive to give the answer.

Operations for Chronic Simple Glaucoma.—The procedure of choice was trephining in 177 instances, basal iridectomy in 39 instances, iridencleisis in 18 cases, a modified Lagrange operation in 18 cases and cyclodialysis in 13 cases. The remaining, miscellaneous procedures included cataract extraction incident to, or complicating, the glaucoma.

A STUDY OF THIRTY-FIVE PATIENTS WITH CHRONIC SIMPLE GLAUCOMA

These patients were selected especially because one eye was treated surgically and the other medically. Both eyes had comparable vision when the patient was first seen.

An opportunity was afforded in this group to study the relative merits of surgical and medical care of chronic simple glaucoma. Most of the patients were observed at a time when the visual acuities of the

eyes were similar, or nearly similar. It appears from the records that the choice of operation was based on the condition of the eye having the higher intraocular tension. It is commonly believed that a high intraocular tension which cannot be reduced by medical treatment is ample cause for surgical intervention. It appears that the loss of vision and the loss of fields were not in themselves decisive factors in making the decision for surgical treatment. In many eyes which were not operated on the tension was much above normal and the fields were severely contracted. There may be instances in which the fellow eye was not treated surgically because the result in the eye operated on was not good.

Of the 35 surgically treated eyes, vision in 30 was worse after operation. Of the 35 medically treated eyes, visual acuity was the same in 20 and better in some others. In the majority of eyes intraocular tension was above normal. Of the 35 surgically treated eyes, 32 had initial vision which was excellent or good, as compared with 11 in which the final vision was excellent or good. Three eyes were listed as partly blind or as blind when initially observed. Twenty-four eyes were listed as blind or partly blind as a final outcome of glaucoma for which surgical measures were part of the treatment.

In 32 of the 35 medically treated eyes, vision was listed as excellent or good in the initial period of observation. For 26 eyes the final outcome of medical treatment was indicated as excellent or good. For 3 eyes the initial vision was blindness or partial blindness at the onset of observation and for 9 the final vision was in this category. It is not to be deduced from this selected series of 35 cases that surgical treatment in itself was responsible for such poor results, as compared with the medically treated eye of the same patient. As stated previously, the surgical procedure may contribute to the damage to an already injured eye. Surgical treatment of chronic simple glaucoma is a mechanical measure to reduce the intraocular pressure. It works very well for acute glaucoma, but poorly for chronic simple glaucoma. These statistics indicate that the present approach to the treatment of chronic simple glaucoma is far from satisfactory. Perhaps additional experimental treatment with newer tension-reducing drugs, such as di-isopropyl fluorophosphate (DFP) or furmethide® (furfuryl trimethylammonium chloride) may be of some service in preparing the eye for a surgical procedure.

Although Elliot trephining is the operation of choice, it is far from satisfactory in the restoration of vision, despite the fact that it reduces intraocular tension. Perhaps the location or site of the operation for the drainage of the intraocular tension should be changed to a less dangerous part than the corneoscleral junction, where so many surgical accidents occur.

Summary.—In the study of 35 selected cases in which one eye was operated on and the other was not, the eye operated on did badly. In view of our personal experience and the statistical analysis, the prevention of poor results in treatment of chronic simple glaucoma points to the need for early diagnosis and early treatment. Many elderly patients may be treated medically in view of their short life expectancy. Surgery is an aid in many instances in postponing the final day of complete blindness.

There is no prescribed formula for the disease, but there should be one for the individual patient.

Thirty-five cases were observed by physicians at the Wills Hospital, for periods of from one to fifteen years. This series was a carefully selected one, in which the diagnosis was made early and patients were observed and followed in a glaucoma clinic. Of 35 eyes operated on, 30 had poorer final vision than when they were first observed. Of 35 eyes not operated on, 25 maintained useful vision. This small series in itself indicates that there is much to learn about chronic simple glaucoma. There certainly must be if the incidence of blindness from chronic simple glaucoma is to be reduced.

SUMMARY

Six hundred and thirty-eight cases of primary glaucoma were studied, with the following distribution:

Chronic simple glaucoma	480 (300 medical, 180 surgical)
Chronic congestive glaucoma	31 (26 surgical, 5 medical)
Acute congestive glaucoma	86 (67 surgical, 19 medical)
Absolute glaucoma	31 (unilateral)
Buphthalmos	10

Seventy-five per cent of the total series of cases of glaucoma were of chronic simple glaucoma; 14 per cent were of chronic congestive glaucoma, and 5 per cent were of acute congestive glaucoma. The rest of the cases were divided between buphthalmos (10 cases) and absolute glaucoma (31 eyes).

In the first survey (1925 to 1936) chronic simple glaucoma contributed 72.3 per cent of the cases, whereas congestive glaucoma contributed 27.7 per cent. In the present series 19 per cent were of the acute and chronic congestive type. If the cases of absolute glaucoma were added to those of the congestive type, this percentage would be raised to 23 per cent, as compared with the 27.7 per cent of the previous survey. In other words, the ratio of cases of acute and of chronic congestive glaucoma is about the same.

It would appear from the two surveys that basal iridectomy is the operation of choice for the congestive type of glaucoma, whereas the Elliot trephination is the preferred methd for chronic simple glaucoma.

In a small group of cases in which chronic simple glaucoma existed in both eyes and in which surgical treatment was carried out on one and medical treatment on the other, it appears that the medically treated eyes did better than the surgically treated eyes. Nearly one half of all the cases studied in this survey were of chronic simple glaucoma in which no operation was performed. Useful vision may be maintained in at least one eye for many years in cases of chronic simple glaucoma with medical care. The first survey showed that in 49 per cent of cases of chronic simple glaucoma tension was reduced by medical treatment alone.

There is no doubt that both surveys point to the need for surgical treatment of acute congestive glaucoma. While some patients are on record who did not receive surgical care, by far the great majority require surgical intervention, especially with the onset of acute pain and rapid loss of vision. The present survey, as well as the first, demonstrates the poor results when the disease is in an advanced stage and visual acuity can no longer be restored. Both surveys point to the need for programs of intensive education, both for the laity and for members of the medical profession, aimed at the discovery of early cases. Glaucoma clinics should be established in every general hospital.

There is need for research for the discovery of drugs which will reduce the tension to satisfactory limits without damage to the eyeball. While there is no complaint concerning the use of physostigmine, pilocarpine, di-isopropyl fluorophosphate or furmethide,* there is a great opportunity for the development of new chemicals.

Basal iridectomy still seems to be the operation of choice for acute glaucoma. There is need, however, for a wider selection of surgical methods in the treatment of chronic simple glaucoma.

Medical methods seem to hold sway in the treatment of a great majority of the cases of chronic simple glaucoma. As long as the etiology is not better known, ophthalmologists will flounder from one surgical technic to another, until something more promising is forthcoming. Great progress has been made in the early diagnosis of the disease, but there is great need for revaluation of the present treatment.

A goodly proportion of members of the ophthalmologic profession, by reason of experience, are extremely conservative in their management of chronic simple glaucoma, preferring to use medical care as long as possible. However, a large number of eyes with chronic simple glaucoma are being operated on earlier. New avenues of approach must be adopted in order to save a greater number of eyes. These new methods call for intensified research on the part of the younger men of the profession.

SCOTOMAS IN CONJUNCTION WITH STREPTOMYCIN THERAPY

Report of Eleven Cases

EDWIN B. THOMAS, M.D.
BOSTON

THE OCCURRENCE of scotoma in the central visual fields during or after streptomycin therapy is presented in 11 cases. In 10 of these cases the patient was being treated for pulmonary tuberculosis, and in 1, for an infection of the urinary bladder with Escherichia coli. In a twelfth case, that of a man who had been treated for pulmonary tuberculosis, there was no field defect. These 12 patients, who had received the full course of streptomycin therapy, represent all persons whose visual fields it was possible to determine.

The only previously reported case of a visual field defect occurring in conjunction with streptomycin therapy is that of Schultz [1]; in this case there was an altitudinal hemianopsia, with subsequent full recovery.

The field defects in the cases reported were of the nerve fiber bundle type and represent a form not previously reported with this therapy.[2] I have not found defects of this type present in routine field examinations of normal persons or in examinations of persons with pulmonary tuberculosis who were not receiving streptomycin.

Traquair [3] stated that defects of the nerve fiber bundle type are not diagnostic of retinal lesions, since the fibers which are close together in the retina continue to lie close together in the optic nerve; such defects

1. Schultz, A. E.: Altitudinal Hemianopsia During Streptomycin Therapy, Am. J. Ophth. **32**:211, 1949.

2. (*a*) Hettig, R. A., and Adcock, J. D.: Studies on the Toxicity of Streptomycin for Man: A Preliminary Report, Science **103**:355, 1946. (*b*) Streptomycin in the Treatment of Infections: A Report of One Thousand Cases, Committee on Chemotherapeutics and Other Agents, National Research Council, J. A. M. A. **132**:4 (Sept. 7) 1946. (*c*) McDermott, W.: Toxicity of Streptomycin, Am. J. Med. **2**:491, 1947. (*d*) Hunter, T. H.: Use of Streptomycin in Treatment of Bacterial Endocarditis, ibid. **2**:432, 1947. (*e*) Farrington, R. F., and others: Streptomycin Toxicity, J. A. M. A. **134**:679 (June 21) 1947. (*f*) The Effects of Streptomycin on Tuberculosis in Man, Report of the Council on Pharmacy and Chemistry, ibid. **135**:634 (Nov. 8) 1947. (*g*) Streptomycin in the Treatment of Tuberculosis, report of the Council on Pharmacy and Chemistry, ibid. **138**:584 (Oct. 23) 1948.

3. Traquair, H. M.: An Introduction to Clinical Perimetry, ed. 5, St. Louis, C. V. Mosby Company, 1946.

are primarily due to pressure or inflammation. They are not found in tobacco, quinine or methyl alcohol amblyopias, all of which tend to reduce visual acuity. The nerve fiber bundle defects may be of such low intensity that colors are necessary for their demonstration. Traquair also stated that arcuate defects, as well as ring scotomas, may develop in retrobulbar neuritis, that nerve fiber bundle defects are rare in chronic retrobulbar neuritis and that the suprachiasmal part of the visual pathway appears to be almost immune to the initial manifestations of toxic and inflammatory disorders of the type that affect the subchiasmal portion.

It has been shown [4] that necrosis occurred in the region of the vestibular nuclei after streptomycin therapy, and it is not inconceivable that this may occur elsewhere in the brain.

The case of Gundrum,[5] in which there was paralysis of a vocal cord during streptomycin therapy, and that of Schultz represent the only cases thus far reported in which damage to any structure other than the eighth cranial nerve has been reported.

That there must be a direct toxic effect on the retinal cells has been shown by Gardiner,[6] since intravitreal administration of streptomycin produced patchy retinal atrophy and pigmentary stippling, without affecting the choroid. No such morphologic changes were found when the streptomycin was given subconjunctivally. No attempt will be made to explain these changes in field on a morphologic basis. Streptomycin however, has been shown to produce increased coagulation of the blood, localized necrosis, specific action on the retinal cells when used locally (and it is conceivable that the same manifestation might occur in a streptomycin-sensitive patient when the drug is given parenterally) and a specific, although ill defined, action on the eighth nerve, producing deafness. It is possible that any one, or a combination, of these four factors could be present to account for these field changes.

REPORT OF CASES

Case 1.—A white man aged 45, who was readmitted to the hospital on Sept. 22, 1947 with far advanced pulmonary tuberculosis, was placed under treatment with streptomycin, 2.0 Gm. by intramuscular injection daily, from October 2 to Jan. 14, 1948; at this time the dose was decreased to 1.0 Gm. daily until February 14, when the drug was discontinued. On about the twenty-eighth day of treatment he began to experience vertigo in bed and dizziness and unsteadiness on arising. In January 1948 he began to complain of blurring of vision and of printed words running together. Refraction showed amblyopia ex anopsia, with vision of 20/200 in the right

4. McDermott,[26] Footnote.[27]

5. Gundrum, L. K.: Paralysis of Left Vocal Cord Following Streptomycin Therapy, J. A. M. A. **138**:22 (Sept. 4) 1948.

6. Gardiner, P. A.; Michaelson, I. C.; Rees, R. J. W., and Robson, J. M.: Intravitreous Streptomycin: Its Toxicity and Diffusion, Brit. J. Ophth. **32**:449, 1948.

eye and a high degree of hypermetropia in the left eye, correctible to 20/20. His complaints persisted after the refractive error was corrected, and on March 19, 1948 the central field of the left eye showed moderate enlargement of the blindspot with a relative pericentral scotoma to 1/2,000 white, about 2 to 4 degrees in radius, with sparing of the central 1 to 2 degrees. The field for 3/2,000 red extended 6

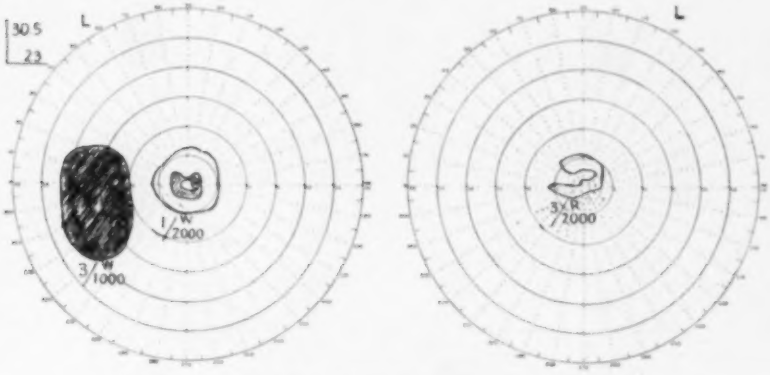


Fig. 1 (case 1).—Visual field (March 19, 1948) of the left eye; visual acuity 20/20 with correction.

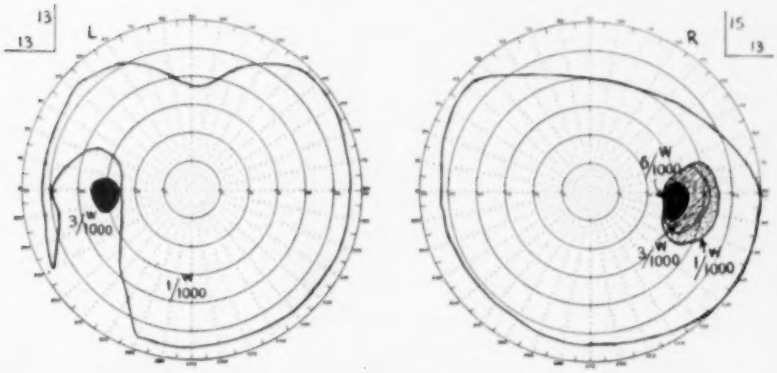


Fig. 2 (case 2).—Visual fields (March 16, 1948); visual acuity 20/20.

degrees superiorly and temporally, with a tonguelike indentation (from the temporal aspect above the fixation point to 3 degrees nasal to and above the fixation point) suggestive of an arcuate defect. Inferiorly this isopter was depressed to within 2 degrees of the fixation point. Determination of the field for the right (amblyopic) eye was unreliable and could not be recorded, owing to the inconsistency of the patient's responses.

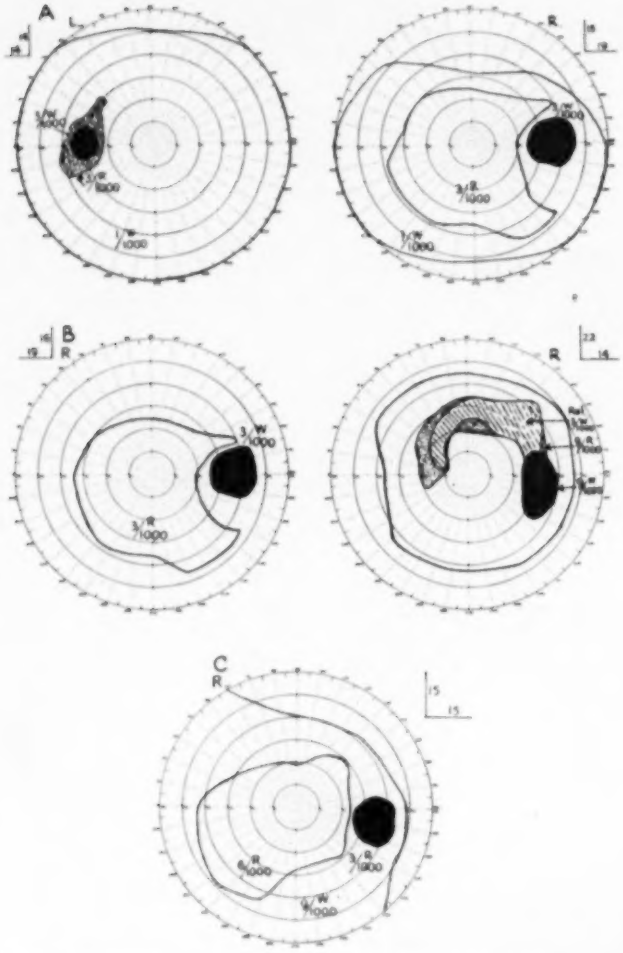


Fig. 3 (case 3).—*A*, visual fields on March 23, 1948; vision 20/15. *B*, visual field of the right eye to 3/1,000 red, on March 23, and of the right eye to 9/1,000 red and 3/1,000 white, on October 15; vision 20/15. *C*, visual field of the right eye on April 19; vision 20/20.

One month later the visual complaints were gone and the central defect could not be found.

Case 2.—A white man aged 35 with advanced bilateral pulmonary tuberculosis was placed under treatment with streptomycin, 2.0 Gm. given daily by intramuscular injection, from July 28, 1947 to Oct. 27, 1947, when the drug was discontinued.

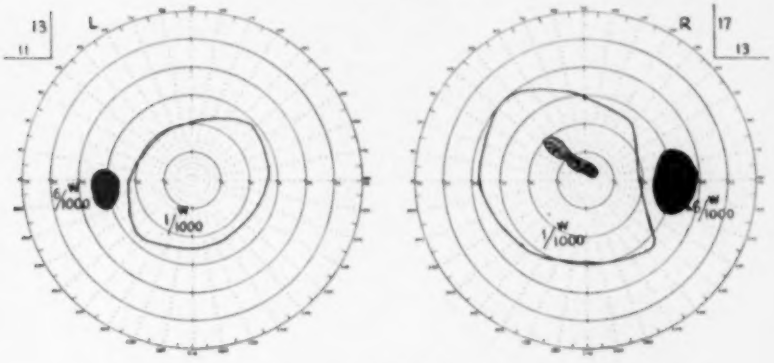


Fig. 4 (case 4).—Visual fields on May 26, 1948; visual acuity 20/30 in the left eye and 20/25 in the right eye.

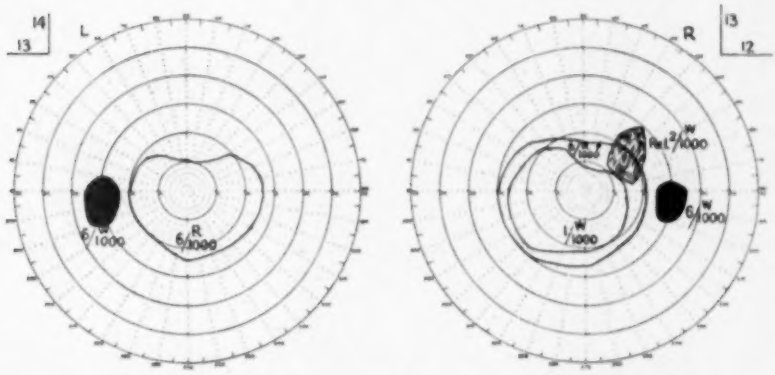


Fig. 5 (case 5).—Visual fields on July 31, 1948; visual acuity 20/40 in the left eye and 20/50 + in the right eye.

Nausea and vomiting developed shortly after he began treatment, and on the tenth day he had a generalized rash, bilateral conjunctivitis and moderate deafness. There was complete and rapid relief of these symptoms with use of tripelennamine ("pyribenzamine"), but the deafness and some dizziness persisted after the tripelennamine was stopped. He had periodic alcoholic bouts, being drunk about one week

a month, and smoked one package of cigarets daily. Vision was correctible to 20/20 in each eye, with a minor refractive error. Determinations of the central fields on March 16, 1948, about five months after he had discontinued streptomycin therapy, showed a normal blindspot to 6/1,000 white in the right eye with temporal enlargement to smaller objects, and, in the left eye, a scotoma to 1/1,000 white breaking through to the inferior temporal periphery.

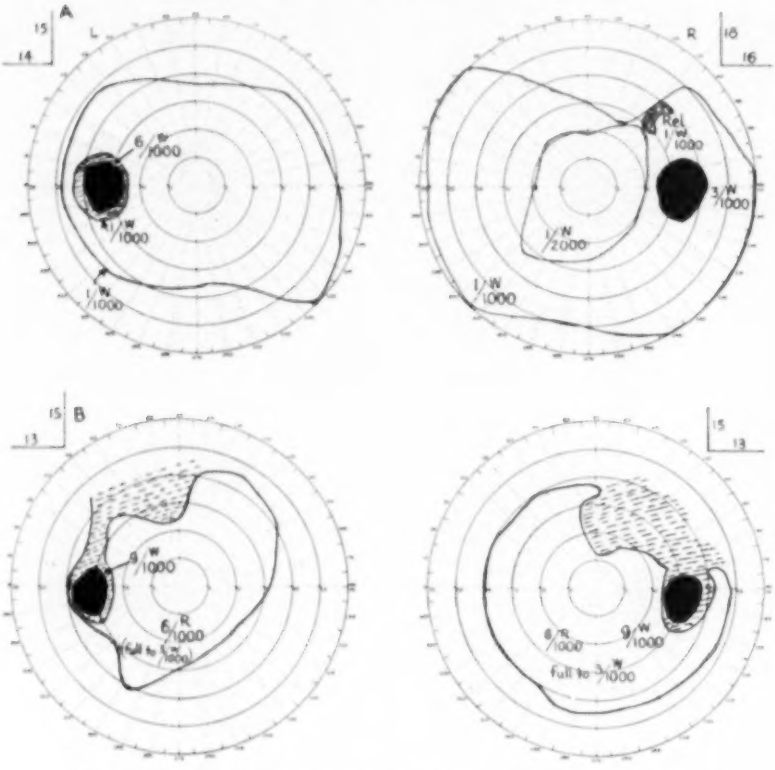


Fig. 6 (case 6).—Visual fields (*A*) on May 27, 1948 (vision 20/20) and (*B*) Oct. 26, 1948 (vision 20/15).

Case 3.—A white man aged 25 with far advanced pulmonary tuberculosis, for which thoracoplasty had been performed, was placed under treatment with streptomycin, 2.0 Gm. daily by intramuscular injection, from July 2 until Oct. 2, 1947; the dose was then reduced to 1.0 Gm. daily from Nov. 23, 1947 until March 19, 1948, when the drug was discontinued. There were vertigo, dizziness and tinnitus, beginning in mid-July 1947. The vertigo and dizziness lasted about one and one-half months and then disappeared, but the tinnitus continued. He also complained of transient episodes of intermittent blurring of objects, "as though they went out

of focus and then became clear," occurring for two months after the onset of vertigo. He received streptomycin, 1.0 Gm. daily, from May 6, 1948 until June 18, 1948, after which its use was discontinued.

The fields on March 23, 1948 showed bilateral enlargement of the blindspot with a small arcuate scotoma to 3/1,000 red extending into the upper temporal field of the left eye. On October 25, after more than five months without streptomycin, the field of the right eye showed a large arcuate scotoma to 9/1,000 red and a similar, slightly smaller and relative, scotoma to 3/1,000 white extending from the blindspot up to and around the fixation point to the horizontal meridian. No deviation from the normal could be made out in the left eye. On Nov. 12, 1948 there was sudden onset of blurred vision with a positive scotoma in the right eye, which cleared in forty minutes. Twenty minutes after onset there was a relative pericentral scotoma to 3/1,000 white; this scotoma was not present twenty minutes later. During this episode, the blindspot initially was 8.5 by 12 inches (21.6 by 30.48 cm.) and later was 6 by 7 inches (15.3 by 17.8 cm.).

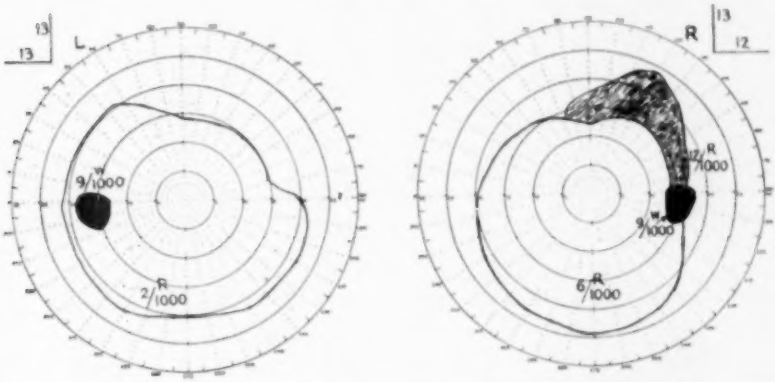


Fig. 7 (case 7).—Visual fields on Jan. 18, 1949; vision 20/20 with correction.

Case 4.—A man aged 47, a former prisoner of war of the Japanese, was discovered to have pulmonary tuberculosis on his release in September 1945. Treatment was started with intramuscular injections of 1.0 Gm. of streptomycin daily on Dec. 18, 1947 and was continued until April 26, 1948. After about three weeks of this therapy he complained of some blurring of vision, unrelieved by refractive correction to 20/20 for distance and to 14/14 for near (Jaeger type). He admitted to eleven years of steady drinking, but had not drunk habitually during the past five years. He smoked one package of cigarets daily. On May 26, 1948, one month after the discontinuance of streptomycin therapy, the central field in the right eye showed a minor enlargement of the blindspot and a narrow ovoid, relative scotoma to 1/1,000 white, 2 degrees above the fixation point and extending along the 45 degree meridian diagonally into the upper nasal field as far as the 10 degree isopter. There was a depression of this isopter in the upper temporal field. The left eye showed a normal blindspot and a depression of the upper temporal field to 1/1,000 white extending from the region of the blindspot across the midline to the 135 degree meridian.

Case 5.—A white man aged 23 with pulmonary tuberculosis and cavitation was placed under treatment with streptomycin, 1.0 Gm. given daily by intramuscular injection, from Dec. 15, 1947 to April 14, 1948, and again from May 23 to June 17, 1948. There were no symptoms referable to vision or to the eighth nerve. The fields on July 31 showed a relative scotoma in the upper temporal field of the right

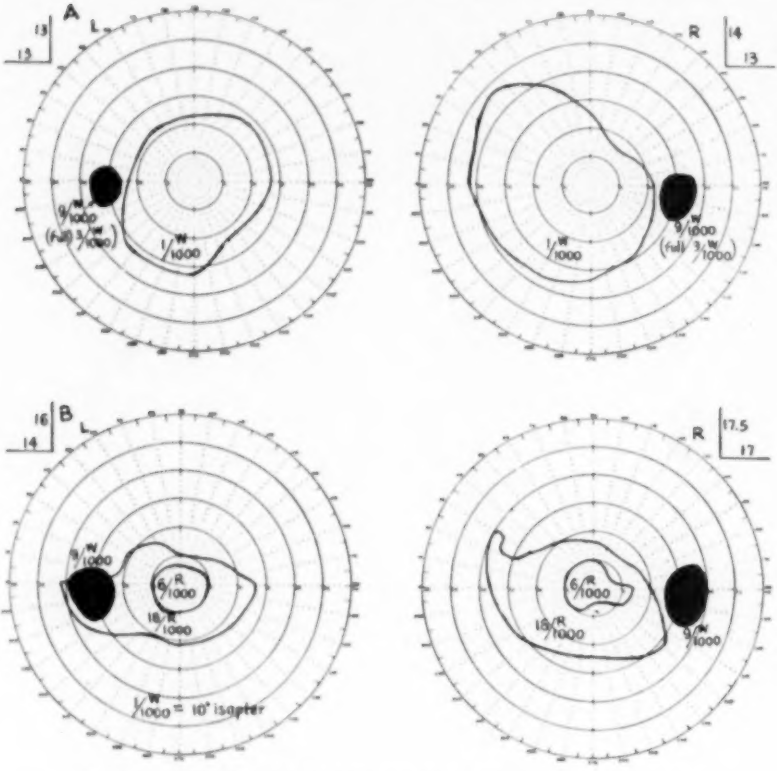


Fig. 8 (case 8).—Visual fields (*A*) July 24 (vision 20/15) and (*B*) Nov. 23, 1949 (vision 20/20).

eye to 2/1,000 white and a depression in the upper temporal area of each eye to 6/1,000 red. Vision was 20/20 uncorrected.

Case 6.—A white man aged 21 with pulmonary tuberculosis and cavitation on Dec. 25, 1947 was placed under treatment with 1.0 Gm. of streptomycin given daily by intramuscular injection and the therapy was continued until April 14, 1948. There were minor symptoms referable to the eighth nerve. About one month after the beginning of this treatment he complained of blurring of vision, which persisted

unchanged until examination on May 27, 1948. The right eye showed a relative scotoma to 1/1,000 white between the 15 and 20 degree isopters and at the 135 degree meridian, the left eye, moderate enlargement of the blindspot. On Oct. 26, 1948 the right eye had an arcuate scotoma to 6/1,000 red, which included the blindspot and arched up into the upper temporal quadrant to just past the midline.

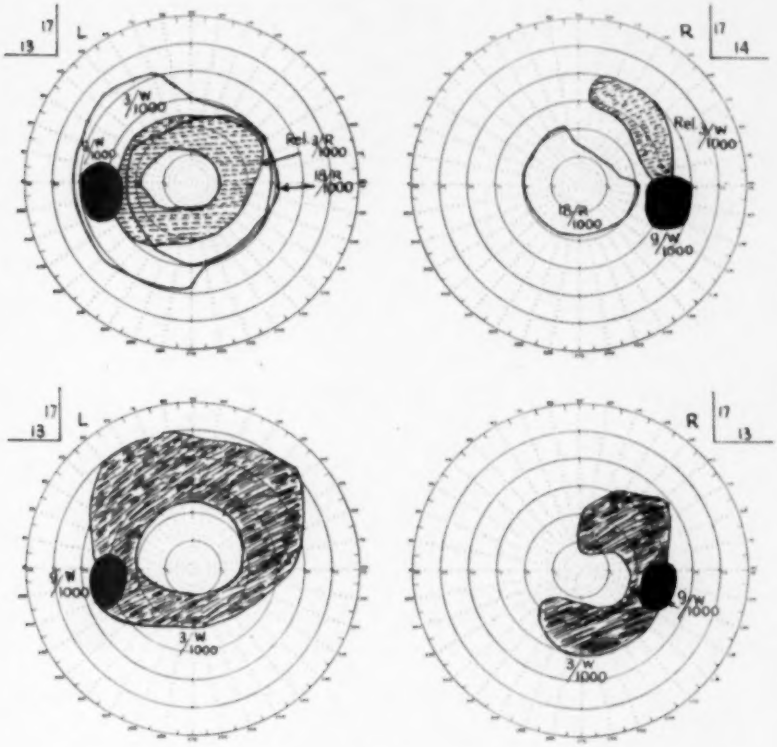


Fig. 9 (case 9).—Visual fields (*A*) March 22, 1949 and (*B*) May 24, 1949. On the former date, vision was 20/20 in the left eye and 20/30 in the right eye; on the latter, 20/20 in the left eye and 20/30 in the right eye.

There was a similar scotoma in the upper temporal quadrant of the left eye. Vision was 20/20 uncorrected, and there was no sensation of blurring at this time.

Case 7.—A white man aged 48 with pulmonary tuberculosis and cavitation received 1.0 Gm. of streptomycin from March 16 until July 19, 1948. He complained of vague blurring of vision while receiving this treatment but had had none since. On Jan. 17, 1949 the central field of the left eye was within normal limits; the

right eye showed an arcuate scotoma to 12/1,000 red extending from the blindspot through the upper temporal quadrant to just past the midline. Vision was 20/20.

Case 8.—A white man aged 40 with moderately advanced pulmonary tuberculosis was given 1.0 Gm. of streptomycin a day intramuscularly from May 26 to Oct. 10, 1948. He noticed symptoms referable to the eighth nerve early in August 1948, and these persisted until examination in November. The fields on July 24,

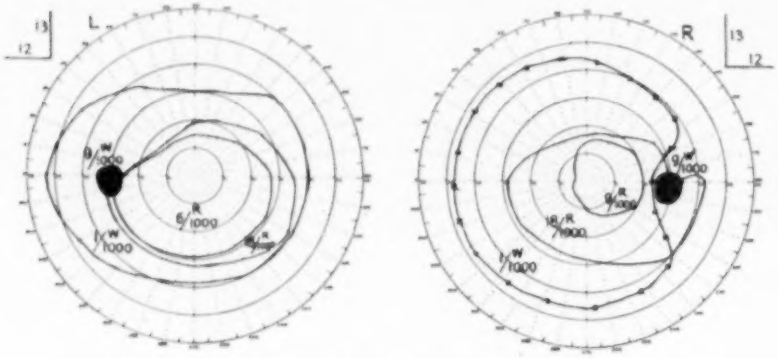


Fig. 10 (case 10).—Visual fields on March 17, 1949; vision 20/20.

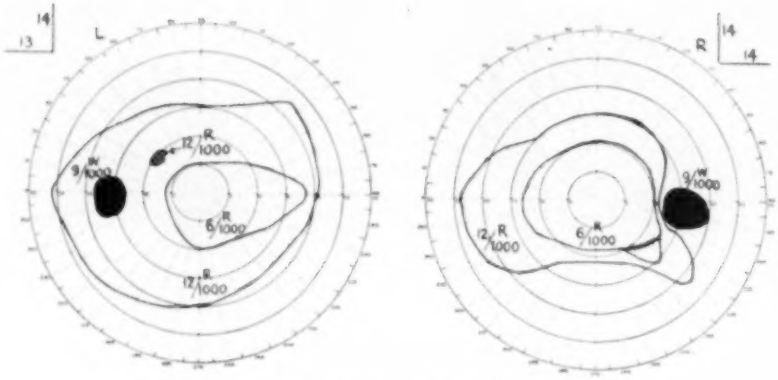


Fig. 11 (case 11).—Visual fields on Feb. 13, 1949; vision 20/20.

1948 showed a depression to 1/1,000 white in the upper temporal quadrant of each eye. Vision was 20/20. On Nov. 23, 1948 each eye showed an arcuate scotoma to 18/1,000 red extending from the blindspot through the temporal into the upper nasal quadrant. Visual acuity was unchanged, and the symptoms referable to the eighth nerve persisted as dizziness on sudden movement.

Case 9.—A white man aged 49 with pulmonary tuberculosis and cavitation received treatment with streptomycin, 1.0 Gm. daily, from Jan. 20 until April 8, 1949.

There was no visual disturbance or symptoms of eighth nerve involvement. On March 22 the field of the right eye showed a relative arcuate scotoma to 3/1,000 white extending from the blindspot almost to the midline, and that of the left eye, a double arcuate relative scotoma to 3/1,000 white, with sparing of the central 5 degree isopter. Each eye showed a depression in the upper temporal quadrant to 18/1,000 red. Vision was 20/20, corrected. On May 24, one and a half months after discontinuation of streptomycin, the right eye showed a relative double arcuate scotoma to 3/1,000 white extending to the midline above and past the midline to the 320 degree meridian below; the left eye showed a complete double arcuate scotoma (relative to 3/1,000 white), which was similar to that of March 22 but slightly larger. Vision was still 20/20, corrected.

Case 10.—A white man aged 36 with pulmonary tuberculosis of seven years' duration began taking streptomycin, 1.0 Gm. daily by intramuscular injection, on Jan. 9, 1949 and continued for sixty-eight days. There were no visual symptoms or disturbances referable to the eighth nerve. Vision was 20/20. On March 17

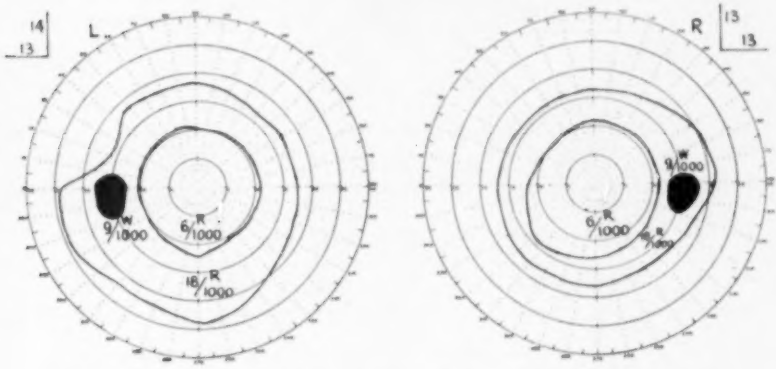


Fig. 12 (case 12).—Visual fields on March 25, 1949; vision 20/20 in each eye.

the fields in each eye showed a scotoma to 18/1,000 red extending from the blindspot up through the temporal quadrant. There was also a depression in the peripheral portion of this isopter in the outer temporal quadrant of each eye.

Case 11.—A white man aged 22 with cystitis due to Esch. coli received 2.0 Gm. of streptomycin daily by intramuscular injection for twelve days, treatment being stopped two days prior to examination of the fields. After the third day he had blurring of vision, itching of the eyes and dizziness. Vision was 20/20. The right eye showed a depression in the upper temporal quadrant to 12/1,000 red, and the left eye, a small scotoma to 12/1,000 red in the upper temporal quadrant with depression in both the upper and the lower temporal quadrant to the same test object.

Case 12.—A white man aged 31 with pulmonary tuberculosis and diabetes began taking streptomycin, 1.0 Gm. a day intramuscularly, on Jan. 5, 1948 and continued until March 6, 1949. There were no toxic symptoms. On March 25 the fields were within normal limits except for a defect to 18/1,000 red in the upper temporal quadrant of the left eye, outside the isopter containing the blindspot.

COMMENT

In all cases the fundi appeared to be within normal limits, as did the tension on palpation.

Summary of Data in 11 Cases of Scotoma Occurring with Streptomycin Therapy

Case No.	Vision	Amount Streptomycin; Duration of Therapy	Time of Field Taking After Treatment, Days	Associated Eighth Nerve Symptoms	Type of Field Change
1	OD : 20/200 OS : 20/20 cc.	2.0 Gm.—105 days 1.0 Gm.— 30 days	179	Moderate, 28th day	OS : Moderately enlarged blindspot; relative peripheral scotoma to 1/2,000 white; small arcuate defect to 3/2,000 red
			209		OS : No defect found
2	OU : 20/20 cc.	2.0 Gm.— 91 days	251	Severe, 10th day	OD : Blindspot enlarged to 6/1,000 white OS : Arcuate scotoma to 1/1,000 white inferiorly
3	OU : 20/20	2.0 Gm.— 93 days 1.0 Gm.—116 days 1.0 Gm.— 43 days	275	Moderate, 13th-58th day	OD : No defect OS : Arcuate scotoma to 3/1,000 red
			491		OD : Large arcuate scotoma to 9/1,000 red; smaller relation scotoma to 3/1,000 white OS : No defect
			559		OD : Positive pericentral scotoma, enlarged blindspot; both transient OS : No defect
4	OU : 20/20 cc.	1.0 Gm.—134 days	174	None	OD : Relation ovoid scotoma to 1/1,000 white, diagonally above fixation OS : Depression in upper temporal field to 1/1,000 white
5	OU : 20/20	1.0 Gm.—130 days 1.0 Gm.— 25 days	228	None	OU : Depression in upper temporal field to 6/1,000 red OD : Relative scotoma in upper temporal field to 2/1,000 white
6	OU : 20/20	1.0 Gm.—110 days	153	Minor	OD : Relative scotoma to 1/1,000 white OS : Moderately enlarged blindspot OU : Arcuate scotoma to 6/1,000 red
			266		
7	OU : 20/20	1.0 Gm.—125 days	307	None	OD : Arcuate scotoma to 12/1,000 red OS : No defect
8	OU : 20/20	1.0 Gm.—137 days	57	Moderate, 71st-179th day	OU : Depression in upper temporal quadrants to 1/1,000 white
			179		OU : Arcuate scotoma to 18/1,000 red
9	OU : 20/20 cc.	1.0 Gm.— 79 days	61	None	OD : Relative arcuate scotoma to 3/1,000 white OS : Relative double arcuate scotoma to 3/1,000 white OU : Depression in upper temporal quadrants to 18/1,000 red
			124		OD : Relative double arcuate scotoma to 3/1,000 white OS : Relative complete double arcuate scotoma to 3/1,000 white
10	OU : 20/20	1.0 Gm.— 78 days	67	None	OD : Depression in upper temporal quadrants to 18/1,000 red
11	OU : 20/20	2.0 Gm.— 12 days	14	None	OD : Depression in upper temporal quadrants to 12/1,000 red OS : Small scotoma in upper temporal quadrant to 12/1,000 red

In none of these cases was the visual acuity not correctible to 20/20 except in one amblyopic eye. However, in 6 cases there was vague "blurring of vision," which disappeared in a short time whether or not the patient was still receiving streptomycin, and this blurring was not associated with sudden movements of the head.

It is interesting to note that in cases 3, 6 and 8 there was initially at best a depression in the upper temporal quadrant, followed in seven,

six and four months, respectively, by the presence of a well defined arcuate defect, and that there were no visual disturbances when the latter were present. In case 3 no streptomycin had been received for seven months; in case 6, none for six months; in case 8, none for one month.

The most frequently encountered scotoma was an arcuate defect in the upper temporal quadrant for red, and occasionally a relative scotoma for small white test objects. This scotoma was in contact with the blind-spot in all 8 cases in which it was fully developed, and it resembled a defect of nerve fiber bundle type.

SUMMARY

Eleven cases are presented in which changes in the visual fields occurred during or after administration of streptomycin. The most frequently observed change was a nerve fiber bundle type of scotoma.

United States Marine Hospital, 77 Warren Street.

OCULAR LESIONS INDUCED BY ACUTE EXPOSURE OF THE WHOLE BODY OF NEWBORN MICE TO ROENTGEN RADIATION

EGON LORENZ, Ph.D.
AND
THELMA B. DUNN, M.D.
BETHESDA, MD.

MUCH HAS been written concerning cataract formation in experimental animals and in man following local roentgen and radium irradiation of the eye. The literature on this subject was exhaustively reviewed by Desjardins [1] in 1931 and by Warren [2] in 1943. Since most of the experimental work was published in the early part of the century, many of the data given on dosage and other conditions of irradiation cannot be reliably interpreted in terms of present standards. Nevertheless, the following effects were clearly established: 1. Irradiation often produces an irreversible opacity of the lens. 2. The lens is considerably more radiosensitive in immature, rapidly growing animals than in mature animals. 3. In immature animals irradiation frequently affects not only the lens but also the retina, while in mature animals only the lens is affected. In 1942 Poppe [3] described experiments in which the eyes of adult rabbits were exposed to a dose of 1,500 r, and the progressive changes in the eyes were studied from twenty-four hours to fourteen months after exposure. He concluded that the cataract seemed to be produced by a direct effect of the radiation on the lens. No changes were observed in the uvea, the retina or the optic nerve except for slight hyperemia of the vessels.

In the present experiment, data are given on the effects on the eye of exposure of the whole body of newborn mice to roentgen rays. These experiments were undertaken to study the general biologic effects of

This paper is based largely on work performed under contract W-31-109-eng-38 for the Manhattan Project at the Argonne National Laboratory.

1. Desjardins, A. U.: Action of Roentgen Rays and Radium on the Eye and Ear, Am. J. Roentgenol. **26**:639-679; 787-819; 921-942, 1931.

2. Warren, S.: Effects of Radiation on Normal Tissue, Arch. Path. **35**:304-353 (Feb.) 1943.

3. Poppe, E.: Experimental Investigations of the Effects of Roentgen-Rays on the Epithelium of the Crystalline Lens, Acta radiol. **23**:354-367, 1942.

irradiation on newborn mice. The changes which were uniformly found in the eyes of these animals were unexpected and striking. For this reason, they are presented in a separate report.

EXPERIMENTAL PROCEDURE

Twenty-four male and 32 female mice of strain A[4] were used as experimental animals, and corresponding numbers served as controls. The controls were obtained by breeding the mothers from which the experimental animals were derived to the same fathers immediately after weaning of the experimental animals. All animals were kept on "purina dog chow" and water *ad libitum*. The experimental litters were given a single irradiation within twelve hours after birth in an open shallow plastic box. The factors of irradiation were as follows: 186 kilovolts, 20 milliamperes, added filtration 0.25 mm. of copper and 106 mm. of aluminum, distance from focus to middle of mouse 50 cm., rate 57 r per minute, total dose 400 r ± 5 per cent. None of the irradiated animals died before they were weaned. The experiments were terminated twelve months later, when both irradiated and nonirradiated animals were killed and autopsied.

RESULTS

Prior to the date on which the experiment was terminated, 8 males and 12 females of the experimental animals died, most of them of leukemia induced by radiation. No instance of leukemia was observed at autopsy in the experimental mice surviving twelve months. Five male and 1 female mouse of the nonirradiated controls died prior to the termination of the experiment. Only 1 mouse with leukemia was found in the control series. In mice with leukemia, an infiltration of leukemic cells has rarely been found around the optic nerve, but this is easily distinguished from the damage due to irradiation, to be described.

The growth of the experimental animals is shown in the weight curves (fig. 1), and those that survived to 12 months of age were vigorous and in good health, although they must have been blind. No lesions of the eye were observed in any of the control mice; on the other hand, opacity of the lens was found in some of the irradiated animals as early as 4 months of age. All experimental mice surviving to 12 months of age (17 males and 22 females) showed lesions in one or both eyes in varying degrees. The eyes of 15 males and 16 females were used for gross dissection, photographs or microscopic sections. Since lesions of the eye were not anticipated when the experiment was planned, no observations on the progression of the lesion were made.

When the eye was examined under the dissecting microscope, the most frequent change was central opacity of the lens. The two eyes were not always similar, and in occasional animals one eye showed only slight clouding of the lens. A few eyes were considerably smaller than

4. The possibility exists that some of these mice were progeny of an outcross of strain C mice.

might be expected, and there was a distinct opacity involving both the lens and the cornea, which was sometimes vascularized (fig. 2). Some of the eyes were removed, and the lens was dissected under the microscope. This procedure was especially revealing, for it showed that the nucleus of the lens was often stony hard and opaque whereas the outer layers of the lens were abnormally soft, and almost fluid in consistency.

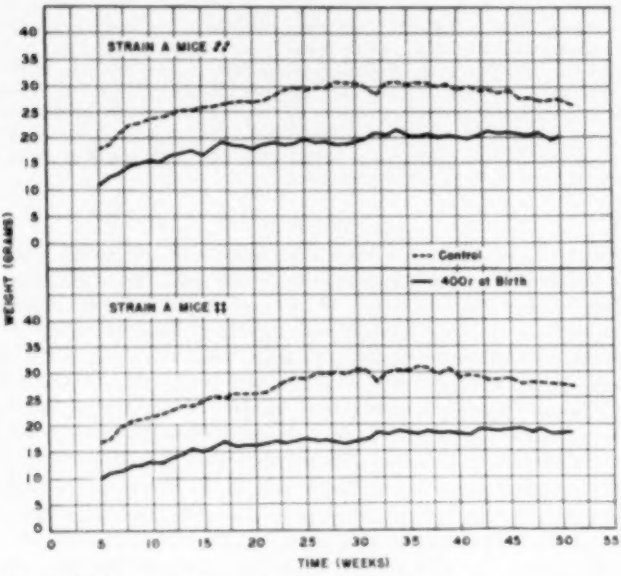


Fig. 1.—Weight curves for nonirradiated (control) and for experimental mice irradiated at birth.

The eyes damaged by irradiation were difficult to prepare for histologic study because of the variation in density in different portions of the eye (fig. 3). Histologically the most consistent and severest damage was seen in the retina, which was only a fraction of its normal thickness (fig. 4). Almost no nuclei were present in the outer nuclear layer; the layer of rods (no cones are found in the eye of the mouse) was absent. The inner nuclear layer was reduced in thickness, and there was relatively little injury to the ganglion cell layer. The lens capsule sometimes appeared thickened; the nucleus of the lens was strongly acidophilic, and 1 specimen contained small calcific deposits. The outer portion of the lens usually appeared vacuolated, and the small spaces

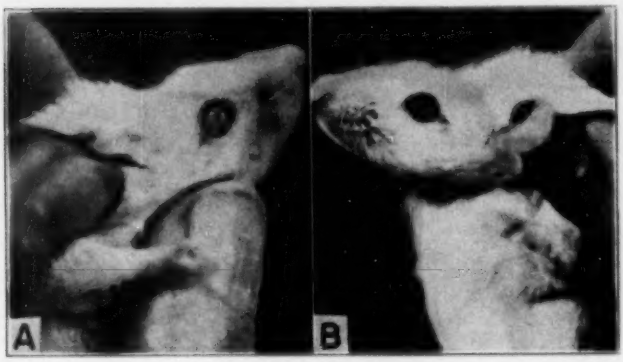


Fig. 2.—*A*, eye of mouse irradiated at birth, as compared with control, *B*.

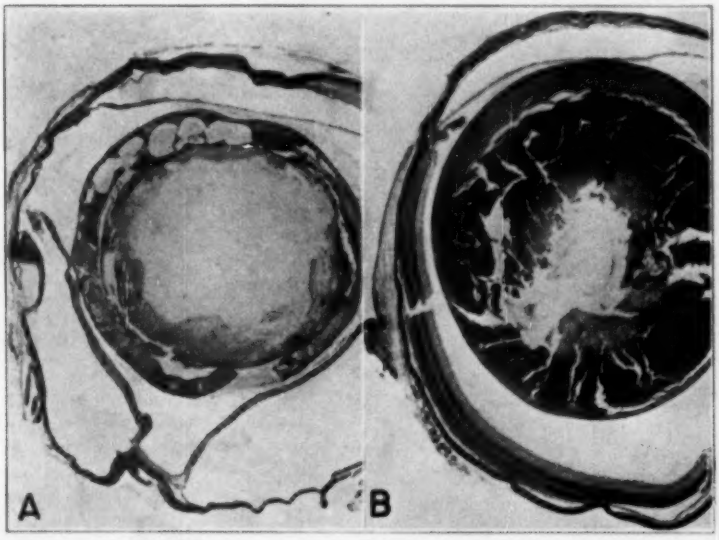


Fig. 3.—*A*, whole cross section of eye of mouse irradiated at birth, as compared with control, *B*. Note atrophy of retina and vacuolation of outer portion of lens. Hematoxylin and eosin; × 28.

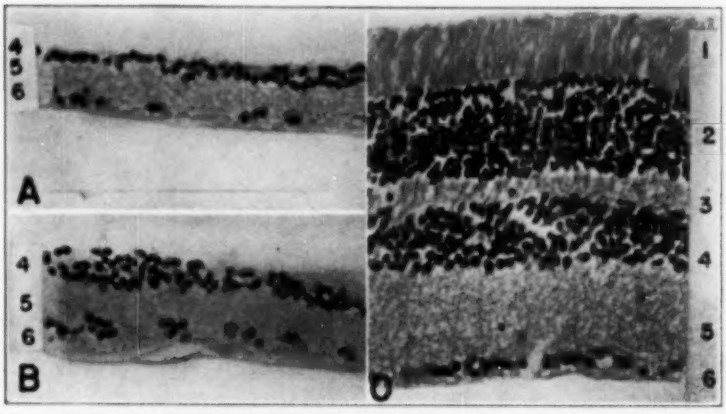


Fig. 4.—*A* and *B*, retinas of mice irradiated at birth, as compared with control, *C*. Note absence of layer of rods, absence of outer nuclear layer, reduced number of nuclei in inner nuclear layer and the ganglion cell layer. *1* indicates layer of rods; *2*, outer nuclear layer; *3*, outer plexiform layer; *4*, inner nuclear layer; *5*, inner plexiform layer; *6*, layer of ganglion cells. Hematoxylin and eosin; × 300.

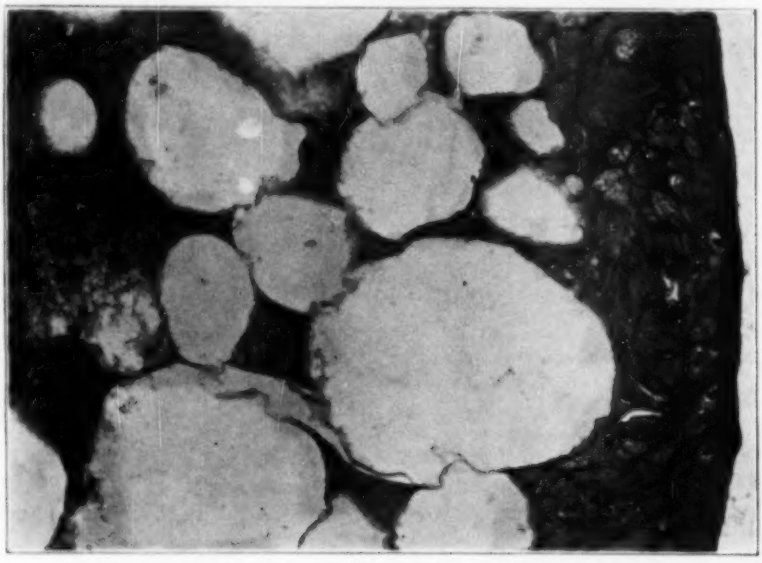


Fig. 5.—Margin of lens of mouse irradiated at birth. Note vacuolation. Hematoxylin and eosin; × 300.

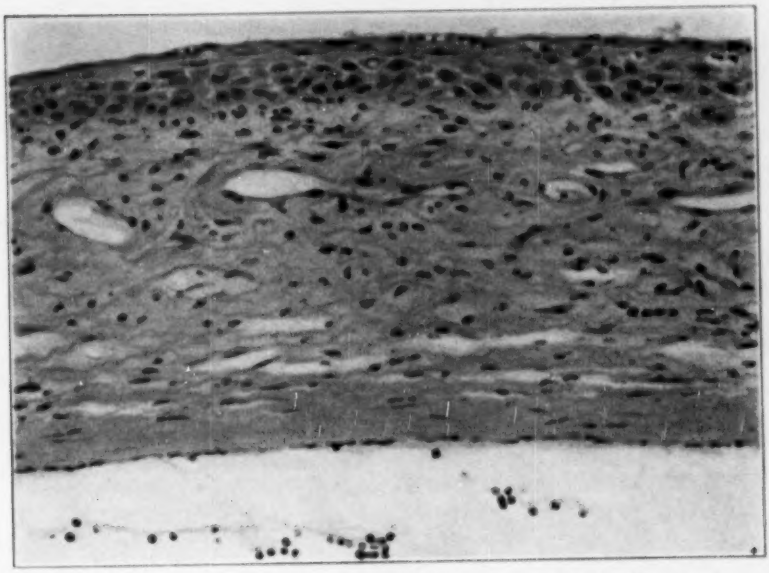


Fig. 6.—Cornea of mouse irradiated at birth. Note vascularization, fibrosis and leukocytic infiltration. Hematoxylin and eosin; × 300.

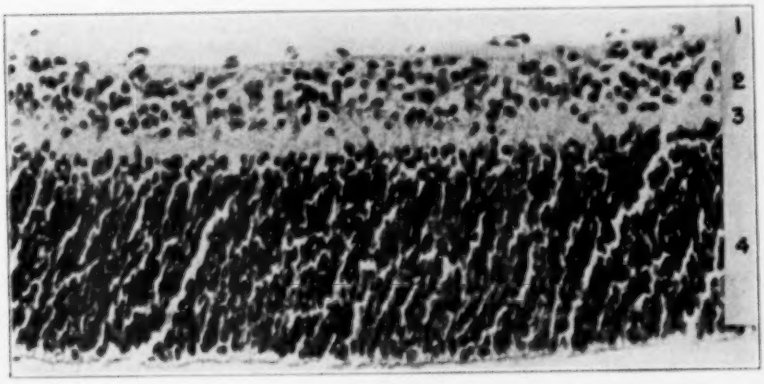


Fig. 7.—Retina of newborn mouse. *1* indicates vascular layer; *2*, layer of nerve cells; *3*, inner molecular layer; *4*, outer undifferentiated layer. Hematoxylin and eosin; × 300.

seemed to be filled with fluid (fig. 5). The cornea generally showed a slight thickening of the surface epithelium and sclerosis of the substantia propria. A few specimens presented areas of vascularization and inflammatory cell infiltration (fig. 6). The iris and ciliary body appeared generally unaltered. The optic nerve was observed in a few sections, and no abnormality was found. A few of the most severely damaged eyes showed areas of old hemorrhage, in which macrophages containing hemosiderin were present in the posterior chamber.

Sections of the eye of normal newborn mice revealed that the eye was not fully developed (fig. 7). Blood vessels were still present on the posterior surface of the lens, and the retina contained an outer undifferentiated layer, such as appears in the human embryo at 4 months.

COMMENT

The injury to the lens, and especially to the retina, of newborn mice caused by irradiation of the whole body is striking, considering that the dose delivered to the eye is rather small (400 r). There is general agreement in the literature that the eye of the adult animal is fairly radioresistant and that a dose to the eye considerably larger than 400 r is necessary to induce opacity of the lens [5] with no apparent injury to the retina. In adult mice of strain A given radiation of the whole body (in ten divided doses) at 2 months of age, no gross opacity of the eye was found at 12 months of age.[6] Likewise, continuous irradiation of the whole body over the entire life span of adult mice, guinea pigs or rabbits started at 3 to 5 months of age failed to induce ophthalmic lesions, although accumulated doses amounted to approximately 6,000 r for mice and guinea pigs and 12,000 r for rabbits.[7]

Although the experimental animals were stunted in growth, all organs appeared histologically normal with the exception of the gonads, which showed atrophy at 12 months of age. However, the gonads are the most radiosensitive organs in the mouse at any age. In general, primitive cells and rapidly dividing cells belong to the most radiosensitive cells, although there are exceptions to this rule.[8] According to Triboudeau and Belley,[9] the difference in sensitivity between the lens of

5. Desjardins,[1] Warren,[2] Poppe.[3]

6. Unpublished data.

7. Lorenz, E.; Heston, W. E.; Eschenbrenner, A. B., and Deringer, M. K.: Plutonium Project: Biologic Studies in the Tolerance Range, Radiology **49**:274-285, 1947, National Nuclear Energy Series, New York, McGraw-Hill Book Company, Inc., 1949, div. 4, vol. 22B.

8. Bloom, W.: Histopathology of Irradiation, from External and Internal Sources, National Nuclear Energy Series, New York, McGraw-Hill Book Company, Inc., 1948, div. 4, pp. 753-754.

9. Triboudeau, L., and Belley, G.: Action des rayons X sur L'œil en voie de développement, Arch. d'electric. méd. **15**:907-918, 1907.

the young and that of the adult is explained by the fact that in the young lens the epithelial cells are in a state of active proliferative growth, whereas in the adult animals their role is purely nutritive. The effect of the irradiation on the retina of newborn mice may be explained on the same basis. Nerve tissue is known to be one of the most radioresistant structures. However, there are scattered reports in the literature [9] that nerve tissue of young animals is less radioresistant than that of mature animals. As stated before, the retina of a normal newborn mouse is not fully developed and contains an outer undifferentiated layer. It is probable that this immature state of development accounts for the radiosensitivity of the retina.

The question arises whether, in addition to a direct effect on the eye, there may be an indirect (systemic) effect because the animals were given radiation to the whole body. Although the animals were dwarfed, they behaved like normal animals, indicating that the central nervous system was undamaged. Walter [10] was unable to find macroscopic or microscopic changes in the brains of young animals (dogs, rabbits and sheep) as a result of injury from irradiation. However, they showed abnormalities in development. It seems unlikely therefore that any indirect effect is of major importance in the pathogenesis of the ophthalmic lesions. However, this point can be proved only by further experimentation.

SUMMARY

Twenty-four male and 32 female mice of strain A were given a single dose of 400 r to the whole body at birth. The experiment was terminated twelve months later. Seventeen males and 22 females survived. All showed lesions in one or both eyes. These lesions consisted of opacity of the lens, partial opacity and vascularization of the cornea and atrophy of the retina, which was only a small fraction of its normal thickness.

The difference in radiosensitivity of the eye of young and that of old animals is discussed.

National Cancer Institute.

10. Walter, R.: Ueber Wachstumsschädigungen junger Tiere durch Röntgenstrahlen, Fortschr. a. d. Geb. d. Röntgenstrahlen **19**:123-142, 1912-1913. Meyer, H.: Lehrbuch der Strahlentherapie Berlin, Urban & Schwarzenberg, 1925, vol. 1, p. 791.

TREATMENT OF OCCLUDED NASOLACRIMAL DUCTS IN INFANTS

MARTIN P. KOKE, M.D.
SAN DIEGO, CALIF.

THE TREATMENT of occluded nasolacrimal ducts in infants apparently needs more discussion, for within sixty days the ARCHIVES published two articles advocating diametrically opposed managements of the condition. A brief résumé of these papers should recall the pertinent facts and disagreements on the subject.

Guerry and Kendig [1] reviewed the literature. They found that most of the papers referred to the condition as congenital dacryocystitis or dacryostenosis and suggested that the malady be called congenital impatency of the nasolacrimal duct with or without dacryocystitis. In a study of 200 consecutive, unselected newborn infants, these authors found 12 with congenital "impatency," as manifested by epiphora and the presence of mucopus after pressure over the affected sac. The condition in these 12 patients was treated by the application of penicillin ointment and daily massage by the mother. The average duration of symptoms after the beginning of treatment was 2.3 months. After the initial survey, the authors saw 5 patients who failed to respond to six months of this treatment. The ducts were probed in these cases, and the condition cleared immediately. They found the approach by the superior punctum much easier than that by the inferior punctum because the arc through which the probe must be rotated in entering the nasolacrimal canal was less via the superior punctum. A false passage was frequently created when the inferior punctum was used. After the probe was passed down the nasolacrimal duct, its presence at the inferior orifice was ascertained by passing a submucous elevator beneath the inferior turbinate body until the probe was encountered and a sharp metallic "click" was heard. The authors expressed the opinion that probing is not an office procedure and that general anesthesia is essential. They used general anesthesia to reduce the number of false passages, eliminate the annoyance of a crying infant and permit exploration of the inferior meatus. These authors advocated

Read at a meeting of the Pacific Coast Oto-Ophthalmological Society in April 1949.

1. Guerry, DuP. III, and Kendig, E. L., Jr.: Congenital Impatency of Nasolacrimal Duct, Arch. Ophth. **39**:193 (Feb.) 1948.

a six month trial with massage before resorting to probe. Kendig, a pediatrician in Richmond, Va., stated that he had consulted several pediatricians, who expressed the opinion that conservative treatment should last six months or longer and that no man he consulted was willing to resort to probing before the infant was 6 months of age. In the discussion of this paper, Cassady expressed himself in favor of early probing, as did Goar. J. M. Dunnington expressed the belief that probing should be done only after massage had failed.

Cassady [2] reviewed 100 cases of "dacryocystitis of infancy." He saw 46 per cent of his patients in the third month of life and stated that in his opinion pediatricians did not advocate prolonged conservative treatment because probing cured the condition so easily. The treatment he used in the 100 cases consisted in probing the nasolacrimal duct at the first visit and then irrigating the duct into the nose. Perhaps if he had irrigated before probing, he might have found that the irrigation was sufficient. General anesthesia was not used except in a few instances. He probed the nasolacrimal duct with a lacrimal cannula, and as this instrument penetrated the inferior end of the occluded duct he injected sodium chloride solution to demonstrate that the passage was open. A penicillin solution was then prescribed as eye drops, and the child was brought back in a few days. In 67 cases the symptoms disappeared after one probing. In 10 others they lasted only one week. In the rest of the cases multiple irrigations or probings were required, particularly when disease had persisted more than three months. Cassady had no serious complications from probing in his 100 cases, and he was unable to find any reference in the American or the foreign literature to serious damage as a consequence of this procedure. In a second article [3] he reported that his survey of the literature revealed fifteen papers recommending early probing and eighteen favoring the use of local antiseptics and massage. Famous men in the specialty of ophthalmology were alined on each side of the controversy.

REPORT OF CASES IN PRESENT STUDY

The following evidence is presented in support of early probing for relief of congenital occlusion of the nasolacrimal duct:

Of 116 infants 12 months of age or younger who had an occlusion of the nasolacrimal duct, 102 were treated by probing. The 14 remaining patients were cured by repeated irrigations of the lacrimal drainage channels. In 14 of the cases

2. Cassady, J. V.: Dacryocystitis of Infancy, Arch. Ophth. **39**:491 (April) 1948.

3. Cassady, J. V.: Dacryocystitis of Infancy, Am. J. Ophth. **31**:773 (July) 1948.

it was necessary to probe more than once, and in 3 of these drainage channels were not functioning normally when last seen. One probing was sufficient to produce cure in 88 of the 102 infants.

In every case the complaints of the parents concerning the infant's eye were dated from birth or a few days thereafter. Various antiseptic drops and massage over the lacrimal sac had been applied by the parents, without avail. The chief symptom was epiphora and pus in 74 infants and epiphora only in 42. However, in every case pus in some form appeared at the puncta when the lacrimal sac was irrigated. The ages of the infants when first seen were as follows:

Age, Months	No. of Infants
1	13
2	17
3	16
4	20
5	9
6	10
7	7
8	5
9	6
10	2
11	4
12	7

The patients requiring multiple probings were all 4 months of age or older except for 2 infants, and 1 of these received two probings and the other three. The 3 infants who were not cured after multiple probings were each 12 months old, and, as previously stated, they had had epiphora and pus since the first few days of life.

The majority of infants whose nasolacrimal ducts were opened by repeated irrigations were in the age group of 3 months or younger, but there was 1 such infant of each of the following ages: 4, 5, 7, 8, 11 and 12 months. One infant 4 months old had acute dacryocystitis, as evidenced by swelling, hyperemia and tenderness of the lacrimal sac and surrounding tissue. This infant was treated with drops of a 5 per cent sulfathiazole solution and hot packs for one week. Penicillin was not yet available. Then, after irrigation of the sac with the sulfathiazole solution on two successive days, the duct was probed. No further trouble occurred.

When an infant was seen with symptoms typical of an occluded nasolacrimal duct, it was "mummied" with a sheet and pressure was applied to the region of the lacrimal sac with an applicator or the finger. After as much pus as possible had been expressed, the inferior punctum was dilated with a Ziegler dilator and the lacrimal sac irrigated with a solution of sodium sulfathiazole or penicillin. In every case pus in some form appeared in the washings that appeared around the lacrimal cannula or from the superior punctum, whether or not pressure had revealed its presence. If there was only a moderate or small amount of pus, a no. 1 Bowman probe was passed into the inferior punctum, through the canaliculus, across the sac and down the nasolacrimal canal. This was followed by irrigation, and patency was ascertained by the appearance of fluid at the nostril or by the rapid swallowing of the child. A solution of sulfathiazole, sulfacetimide or penicillin was prescribed for home instillation, and the patient was seen again in one week. At that time, if the symptoms had disappeared and irrigation showed patency, the patient was discharged. In cases in which there was a large amount of pus, irrigation was carried out three or four times at intervals of two or three

days, and the duct was then probed unless it opened from the irrigation. When the first and second probings failed, larger probes, through the no. 6 Bowman probe, were used. Three 12 month old babies had weekly probings over many weeks. At each probing fluid appeared at the nostril, but the ducts failed to maintain patency. In 1 case a false passage was made. The probe apparently broke through the wall of the canaliculus, and fluid appeared in the tissue of the lower lid when the duct was irrigated. The procedure was then carried out through the superior punctum, and no ill effects occurred. In no case was a general anesthetic used. Two drops of 0.5 per cent tetracaine hydrochloride was instilled before the punctum was dilated.

COMMENT

Providing patency to an obstructed nasolacrimal duct is primarily important because it eliminates the infection, which creates a hazardous situation. If the infant sustains a break in the surface of the eye in the presence of infected material from the lacrimal drainage channel, there is a definite possibility that a complication of serious import may ensue. Early cure of the obstruction is desirable, for the longer the condition exists the greater is the possibility that probing will fail and that a more complicated surgical procedure, i. e., dacryocystorhinostomy, may be necessary. Of course, the concern of the infant's family is greatly relieved by a rapid cure of the disorder. Last, but not least, the pediatrician is not harassed for months because the eye drops and the massage he prescribed have not helped.

In none of the cases reported by Guerry and Kendig did treatment with massage and local antiseptics, as prescribed by them, for an average time of 2.3 months, correct the occlusion. As previously stated, they advocated massage and the use of local antiseptics for six months before probing. Why an ophthalmologist with the digital skill to do intraocular surgery should hesitate for six months to probe a nasolacrimal duct is a mystery. What apprehension on the part of the pediatrician leads him to advise against probing for six months is unclear. The hydraulic principles of pressure over the sac were expressed by Crigler [4]; why it should take several months to produce relief is obscure.

From their experience in 5 cases, Guerry and Kendig concluded that the creation of a false passage when the inferior punctum was used resulted because the upward rotation of the probe in the inferior canaliculus was over 90 degrees. This, of course, implied that the false passage was produced after the probe had traversed the canaliculus and lay against the medial wall of the sac. It is somewhat difficult to conceive how a false passage could be created after that part of the maneuver had been completed. The danger of making a false passage exists before the probe reaches the medial wall of the sac.

4. Crigler, L.: Treatment of Congenital Dacryocystitis, J. A. M. A. **81**:23 (July 7) 1923.

In the cases here reported the inferior punctum was used because eversion of the lower lid and exposure of the punctum required only one finger, whereas both hands were necessary to evert the upper lid. In a few cases the probe did not pass through the inferior canaliculus with ease, and in those cases the superior punctum was used. No difficulty arose in rotating the probe to pass it into the nasolacrimal canal.

SUMMARY

Salient differences of opinion, as expressed in papers by Guerry and Kendig [1] and Cassady [2] concerning the treatment of occluded nasolacrimal ducts are presented. The so-called conservative school advocates massage and use of local antiseptics for six months, probing at the age of 6 months to be done in the hospital with the use of general anesthesia. Those of the opposing opinion favor early probing in the office with local or no anesthesia.

Occluded nasolacrimal ducts were probed in over 100 infants, without ill effect. Of 116 infants, 88 were cured by a single probing, 11 by two or more probings and 14 by irrigation, and 3 were not relieved by repeated probings. According to the treatment advocated, the infant is "mummied" with a sheet. The head is held by the nurse while the inferior punctum is dilated and the sac is irrigated until it is free of pus. A no. 1 Bowman probe is passed into the punctum, through the canaliculus, across the sac and down the nasolacrimal duct. The lacrimal passage is then irrigated with a solution of penicillin containing 100,000 units in 15 cc. of distilled water until the fluid appears at the nostril or the child stops crying to swallow. The parents are instructed to use eye drops of a penicillin solution and to bring the child back in one week. In a great majority of cases a cure can be expected.

To probe the nasolacrimal duct is not a radical procedure. There is no justification for permitting symptoms of congenital occlusion of the nasolacrimal duct to persist more than one month. The use of general anesthesia and hospitalization in probing the duct of a child 12 months or younger is unnecessary and expensive and adds a mortality hazard.

233 A Street.

CORNEAL OPACITY ACTING AS A CONCAVE LENS

Report of a Case

SAMUEL L. SALTZMAN, M.D.
NEW YORK
AND
M. ALLEN GREENWOOD, M.D.
STATEN ISLAND, N. Y.

THE PRODUCTION of bizarre optical phenomena by foreign bodies, bullae and scars located in or on the cornea is certainly a common occurrence in ophthalmoscopy; yet references in the literature would seem to be nonexistent. The few articles to be found, such as those of Koby [1] and Berliner,[2] are confined to works on slit lamp examination, and hence are outside the realm of ophthalmoscopy, although similar principles apply.

In the case which follows, we propose to present and explain an unusual shadow produced when an eye with an insignificant macula of the cornea was examined ophthalmoscopically.

REPORT OF CASE

J. V., a 6 year old white boy, was admitted to the pediatric service of the Sea View Hospital for tuberculous pneumonitis of the parahilar segment of the left lung. An ophthalmologic consultation was requested.

External Examination.—Right Eye: A faint, circular macula of the cornea, about 2 mm. in diameter, was situated between the lower border of the pupil and the limbus in the region of 6 o'clock. Examination with the slit lamp revealed that the scar had roughly the contour of a faceted bowl, with its deepest point lying almost exactly at its center. It was noted that a very faint, enlarged image of the scar was cast on the posterior surface of the cornea when the diffuse beam of the slit lamp was used.

Left Eye: An adherent leukoma of the cornea was situated between the lower border of the pupil and the limbus in the region of 6 o'clock.

From the Department of Ophthalmology of the Sea View Hospital, Staten Island, N. Y.

1. Koby, F. E.: Les ombres portées en microscopie oculaire sur le vivant, Arch. d'opht. **41**:271-277, 1924; Slit-Lamp Microscopy of the Living Eye: Early Diagnosis and Symptomatology of Affections of the Anterior Segment of the Eye, translated by C. Goulden and C. L. Harris, ed. 2, Philadelphia, P. Blakiston's Son & Co., 1930, pp. 73-76.

2. Berliner, M. L.: Biomicroscopy of the Eye: Slit Lamp Microscopy of the Living Eye, New York, Paul B. Hoeber, Inc., 1943, vol. 1, pp. 108-111.

Ophthalmoscopic Examination.—Right Eye: With a + 2.00 lens held at a distance of 10 inches (25 cm.) from the eye, the startling shadow shown in figure 1 was seen. A false impression of depth and solidity gave to the shadow the appearance of a cystic body apparently located in the vitreous or springing from the retina. So strong was this impression that a number of competent observers requested studies of the stool for ova and parasites. By means of parallax, however, it was observed that the "cyst" was located anteriorly. Finally it was realized that the entire appearance was due to interference of the corneal scar with the light from the ophthalmoscope.

The fundus was normal.

Left Eye: The media and fundus were normal.

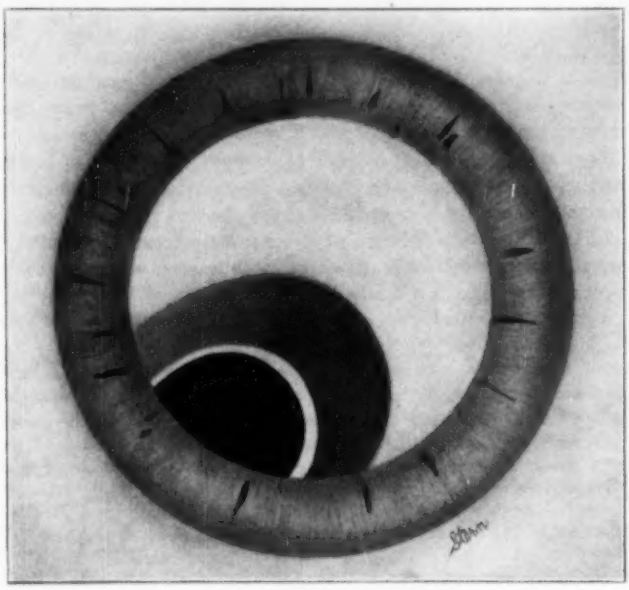


Fig. 1.—Corneal opacity in the right eye acting as a concave lens.

COMMENT

Both the scar of the cornea of the right eye and the adherent leukoma of the left eye were probably the sequelae of phlyctenular keratoconjunctivitis, although no definite history of this disease could be elicited.

Figure 1 shows how the shadow looked to an observer viewing the right eye through the + 2.00 D. lens of an ophthalmoscope held about 10 inches (25 cm.) from the eye. The figure fails, however, to give fully the impression received by all who observed it, i. e., that it was situated deep in the eye and had actual substance.

There are two major factors in the production of such a shadow: (1) the actual configuration of the scar and (2) the varying density of different areas of the scar.

With respect to the first factor, examination with the slit lamp revealed that the scar was hollowed out of the anterior surface of the cornea and was shaped roughly like a bowl. The normally convex anterior surface of the cornea was concave in the area of the scar and, together with the posterior surface of the cornea, formed a concave lens. Figure 2 shows this diagrammatically, with the normal convex anterior surface of the cornea represented as a dotted line. Any concave lens will cast an image of itself, since light rays passing through it are caused to diverge. Hence the area of the projection of the light rays passing through the lens is less bright than the area illuminated by those rays which do not pass through the lens. That this is so may easily be demonstrated. Take a high minus lens from the trial case

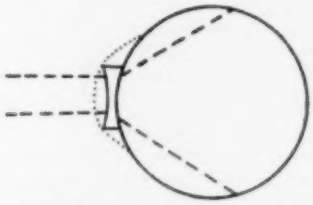


Fig. 2.—Diagram showing how a concave lens was formed in the area of the corneal scar (abnormally concave anterior and normal posterior surface of the cornea).

and hold it above a sheet of white paper. Pass a bright beam of light through this lens and observe the effect on the paper. In the case reported, the concave corneal lens threw an image of the ophthalmoscope light into the eye. This image, which was projected on the intraocular structures (posterior surface of the cornea, iris and anterior capsule of the lens), was less bright than the area of illumination surrounding the shadow, produced by the rays passing through the cornea beyond the scar. Thus, even if the scar were of the same optical density as the clear cornea, it would still produce a relatively less bright area when viewed with the ophthalmoscope.

The second factor, the density of the scar, played a minor role in the final effect. Of course, the factor that most of the scar was thin enough to allow light rays to pass through was essential to its action as a concave lens. The various densities of different areas of the scar so

varied the intensity of the light passing through them as to add to the appearance of solidity of the shadow and reenforce the effect of a concave lens.

334 West Eighty-Sixth Street (24) (Dr. Saltzman).

Sea View Hospital (Dr. Greenwood).

Dr. Abraham Kornzweig, of Mt. Sinai Hospital, New York, and Dr. Arthur Linksz, of the Manhattan Eye and Ear Infirmary, saw the patient and offered valuable comment and criticism.

FREQUENCY OF OCCURRENCE OF CATARACT IN ATOPIC DERMATITIS

ALFRED COWAN, M.D.
AND
JOSEPH V. KLAUDER, M.D.
PHILADELPHIA

IN THIS paper an investigation to determine the incidence of cataract in patients with atopic dermatitis is reported. Such cataracts, first described by Andogsky,[1] were called "dermatogenous cataracts"; this term, however, included cataracts associated not only with atopic dermatitis but with several other dermatoses. Since Coca [2] the term "atopic cataract" has been employed.

There is no report in the literature of the study of a large series of patients with atopic dermatitis (such as is given here) to determine the incidence of atopic cataract. Too few of the reported cases of atopic cataract afford a proper description to justify the conclusion that such cataract is distinctive and can be ascribed to the cutaneous disease. In some reports no mention is made of examination with the slit lamp, and in others the changes in the lens are not described in sufficient detail to convey a proper concept of such change.

Sometimes misleading terms are used. For instance, "central opacities" while the rest of the lens is clear implies that the cataract involves the embryonic or fetal nucleus. Such a cataract must be considered congenital, and therefore not part of the syndrome. Probably what the authors mean is that the opacities lie in the axial portions of the outer zones of the lens. Frequently lesions are said to lie in the "cortex" in persons so young that the cortex, as understood in slit lamp microscopy, is not yet formed. We think "outer zone" a better and more comprehensive term.

The visual acuity is not given in some reports, and often, when it is, is out of all proportion to the degree of loss of transparency of the lens as described. A notation of the visual acuity with the best cor-

Read at the Section on Ophthalmology of the Ninety-Eighth Annual Session of the American Medical Association, Atlantic City, N. J., June, 1949.

1. Andogsky, N.: Cataracta dermatogenes: Ein Beitrag zur Aetologie der Linsentrübung, Klin. Monatsbl. f. Augenh. **17**:824, 1914.

2. Coca, A. F.: Specific Diagnosis and Treatment of Allergic Diseases of the Skin: Present Status, J. A. M. A. **103**:1275 (Oct. 27) 1934.

recting glass is especially important in those cases in which the only indications of cataract are dots or punctate or other opacities, changes which are so common that they can hardly be considered pathologic, certainly not pathognomonic.

Opacities in the embryonic and fetal zones of the lens must be excluded as part of the early stage of acquired cataract. The prominence of the Y sutures cannot be accepted as a sign of beginning cataract; later, however, the increased visibility of the Y's may be due to contrast with the rest of a more relucent lens. Iridescent crystals, which are not part of, or included in, a larger opacity, are also seen in normal eyes. They also are seen in so many different types of cataract that they are not diagnostic.

Bellows [3] described atopic cataract as follows:

> The typical cataract associated with neurodermatitis consists of a characteristic plaque or shield-like opacity in the anterior or posterior cortex. It lies in the pupillary area and at first involves only the most superficial layers of the cortex (Lowenstein, 1934). The capsule may be wrinkled or irregular but is essentially normal. The fully developed cataract frequently appears silver gray, or light cream in color.

The following statement is quoted from Duke-Elder [4]:

> The cataract is typically circumscribed and shield-shaped, limited by concave borders and situated in the anterior cortex. It frequently shows a metallic luster and from it fine linear opacities may radiate peripherally.

Cordes and Cordero-Moreno [5] stated the following opinion:

> What is usually considered a typical form of atopic cataract is the formation of a white milky plaque in the pupillary area which may be localized in the region of either the anterior or posterior pole of the lens, involving the superficial layers of the lens cortex.

According to Brunsting,[6] Benedict stated:

> The earliest changes appear as granular deposits on the inner surface of the anterior capsule or slightly behind the capsule within the cortex. A diffuse grayish translucency intensifies the light beam through the lens. As the opacification increases, the suture lines that make up the anterior and posterior "Y" become more prominent, giving a feather-like appearance. . . . Granular deposits appear at the posterior pole and gradually extend peripherally. . . . As the cataract develops the lens takes on a diffuse grayish appearance. . . . A fully mature cataract is silver gray or light cream.

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3. Bellows, J. G.: Cataract and Anomalies of the Lens: Growth, Structure, Composition, Metabolism, Disorders and Treatment of the Crystalline Lens, 1944, St. Louis, C. B. Mosby Company, p. 472.

4. Duke-Elder, W. S.: Text-Book of Ophthalmology, St. Louis, C. V. Mosby Company, 1941, vol. 3, p. 3220.

5. Cordes, F. C., and Cordero-Moreno, R.: Atopic Cataracts: Report of Four Cases, Am. J. Ophth. **29**:402, 1946.

6. Brunsting, L. A.: Atopic Dermatitis (Disseminated Neurodermatitis) of Young Adults, Arch. Dermat. & Syph. **34**:935 (Dec.) 1936.

Lastly, we quote Beetham [7]:

> Two types of lenticular changes can be described; the first is the typical and commonly seen complicated cataract. This usually begins at the posterior pole of the lens with increased iridescence, vacuoles and precipitates. Striation of the lens fibers is often present; small punctate opacities are common, and iridescent crystals are frequent. These changes spread peripherally, and similar changes are soon noted in the anterior cortex at the pole, immediately beneath the capsule. The changes progress, and the entire cortex becomes cloudy, forming an intumescent or a homogeneous mature cataract. . . . The second type . . . can be described as follows: a dense irregular plaque of opacity in the anterior cortex occupying the pupillary area immediately beneath the capsule.

REPORT OF STUDY

In our investigation, the crystalline lenses of 100 consecutive patients with atopic dermatitis were examined biomicroscopically for the presence of any opacities that could be considered to have been produced after birth. All these persons sought relief primarily for the dermatologic trouble, and the diagnosis of atopic dermatitis was certain in every case. In order to eliminate the probability of senility as an etiologic factor, no one over 40 years of age was included. The youngest patient was 2½ years old, and the average age was 16.4 years. There were 36 males and 64 females. During the course of this investigation 3 persons who had atopic dermatitis, but were over the age limit, were found with cataract that could be considered atopic, but data on them were not included in our statistical material.

In young persons in whom the cortex was not yet formed, the opacities noted were found first either in what may be considered the infantile nucleus or in the adult nucleus or in both. Opacities which are known as congenital, that is, those formed in the parts of the lens present at birth, were not included. Neither included were the peripheral, distinctively characteristic, opacities of coronary cataract. In some instances (with positive findings) examination was repeated and the condition kept under observation over a number of years. For these persons the given age is that when the lesions were first seen.

Control Patients.—For comparison and as a check, 100 run of the office patients of ages comparable to the patients with atopic dermatitis were examined for lenticular opacities. The youngest of these was 3 years of age and the oldest 40 years, the average age being 20.6 years. Among these were 41 males and 59 females. This group included no one in whom there was known evidence of any condition, local or general, that might contribute to the production of cataract.

In this group acquired lenticular opacities were found in 48 (24 per cent) of all eyes and in 28 per cent of all patients examined—in

7. Beetham, W. P.: Atopic Cataracts, Arch. Ophth. **24**:21 (July) 1940.

the anterior portion of the lens in 25 eyes, in the posterior portion in 13 eyes and in both portions in 10 eyes. Of the males 17 per cent, and of the females 37.1 per cent, were affected. The opacities were bilateral in 20 patients (71.4 per cent) and unilateral in 8 (28.5 per cent). The youngest was a girl aged 11, with opacities in both eyes. The youngest male patient was 21 years of age, with opacities in one eye. The average age of all patients with opacities was 25.5 years.

Patients with Atopic Dermatitis.—Of these patients only those with positive signs of acquired lenticular opacities are listed.

Case 1.—C. S., a woman aged 23.

Right Eye: This eye was aphakic, having been operated on for cataract four months previous to her first visit. The pupil was irregular in outline and displaced upward and extended from above the normal position to near the limbus at 12 o'clock. There was no surgical coloboma. The iris showed moderate stromal and retinal pigment atrophy. The pupillary space was filled with a dense gray, vascularized membrane, with numerous clumps of pigment and star figures deposited all over the surface of the membrane. Visual acuity was 6/60 with a correcting glass.

Left Eye: Immediately under the anterior capsule of the lens, and involving it to the extent that the surface of the lens was wrinkled and irregular, was a thin opacity, dense, lustrous and bluish white in the center and thinning out toward the periphery. It extended over the entire pupillary area, and its continuations could be seen over the entire posterior cortex immediately under the posterior capsule. Here, posteriorly, were also a considerable number of iridescent crystals and yellowish, transparent and opaque bodies, giving a modified mother-of-pearl appearance. The lens seemed otherwise unaffected except for a questionable general loss of transparency with diminished visibility of the suture lines and surfaces of discontinuity. Visual acuity was equal to light projection.

Case 6.—C. D., a woman aged 18.

Symmetrically in front of the posterior capsule of each lens was a very thin, yellowish disk, occupying a small area around the axis and containing iridescent crystals and a few vacuoles—the earliest stage of complicated cataract. The lenses were otherwise clear. Visual acuity was 6/6 in each eye.

Case 9.—F. D., a woman aged 24.

In each eye the lens had a general slight reluctancy of the posterior cortex in the vicinity of the pole, with a few yellowish, mother-of-pearl opacities and several iridescent crystals—incipient complicated cataract. The eyes were otherwise normal. Visual acuity was 6/6 in each eye.

Case 11.—G. H., a girl aged 10 years.

There were several tiny whitish dots in the posterior cortex of the lens of each eye. Visual acuity was 6/6 in each eye.

Case 18.—G. L., a woman aged 24.

The right eye showed an irregular, dense, pearly white opacity in the anterior cortex of the lens, considerably elevating the surface of the lens and extending backward through much of the anterior cortex, which was still very narrow, in conformity with the patient's age. Around this dense, irregular opacity, which was probably 2 mm. in diameter, were less dense, whitish, dotlike and radiating linear opacities in various planes throughout the affected area. The deeper portions

of the lens could not be seen distinctly enough to be described. Visual acuity was limited to detection of shadows. The lens of the left eye was clear, and visual acuity in that eye was 6/6 with correcting glass.

Eighteen months later the cataract in the right eye resembled in every respect a mature cortical senile cataract. In the left eye the lens was still clear and the visual acuity unchanged with the same correcting lens.

Case 24.—H. M., a man aged 25.

Fine, glistening, flat, slightly yellowish spots and several vacuoles were grouped in the vicinity of the posterior pole and lay in a narrow plane in the posterior cortex, immediately in front of the posterior capsule of each eye. Visual acuity was 6/6 in each eye.

Case 28.—L. C., a girl aged 16.

Left Eye: Below the center, on the anterior face of the adult nucleus, were several tiny white dots and one larger, but less dense, opacity. Visual acuity was 6/6 in this eye.

Case 29.—L. C. Sr., a woman aged 36.

In the left eye, a number of medium-sized vacuoles were situated in the posterior cortex near the pole, immediately in front of the capsule. There were a few tiny iridescent spots in the anterior cortex. These all had a decided yellowish reflex. In the right eye the lens was clear. Visual acuity was 6/6 in each eye.

Case 31.—C. M., a youth aged 17.

In each eye tiny whitish dots were found in the anterior and posterior subcapsular zones. A few punctate, grayish opacities lay in the neighborhood of the surface of separation between the adult and the infantile nucleus, both anterior and posterior (coronary cataract). Visual acuity was 6/6 + in each eye.

Case 32.—P. P., a youth aged 18.

Right Eye: The first operation for cataract had been performed two years prior to the first visit; another operation had been done one year later. There was a linear scar above; otherwise, the cornea was clear except for a few brown keratic precipitates; the aqueous was empty, and the iris was drawn up and out, with a considerable portion attached to the posterior surface of the cornea. The coloboma was ragged. The iris in general was atrophied, mostly in the vicinity of the coloboma. The pupillary space was filled with a dense white membrane. Vision was limited to light perception.

Left Eye: There were numerous various-sized, but mostly small, irregular-shaped, grayish and dirty white opacities situated in all the layers of both the anterior and the posterior external zone, but so densely in the anterior zone that the posterior portion could be only indistinctly seen. Distributed among these opacities were a few glistening, iridescent crystals. Visual acuity was 6/30.

Case 36.—R. H., a man aged 39.

In each eye there were marked increase in relucency of the anterior face of the adult nucleus and a number of punctate opacities deep in the anterior cortex. Visual acuity was 6/6 in each eye.

Case 39.—H. S., a youth aged 14.

Each eye showed several small, gray dots and fluffy white opacities in the posterior zone in the vicinity of the pole. Visual acuity was 6/6 in the right eye and 6/60 (c. c. squint) in the left eye.

Case 42.—S. M., a woman aged 25.

In each eye there were many round, well defined opacities of a faintly yellowish color, all situated deep in the anterior and posterior portions of the adult nucleus,

chiefly around the periphery, with a few in the axial areas. They varied in size, some being fairly large (0.25 mm.); all were circular, some being disciform and some ellipsoid (coronary). Visual acuity was 6/6 in each eye.

CASE 47.—D. C., a woman aged 22.

A few tiny whitish dots were found in the anterior and posterior cortices in each eye, near the face of the adult nucleus. Visual acuity was 6/9 in each eye.

CASE 48.—J. G., a youth aged 13.

In the lens of each eye were a considerable number of small, dirty white, irregular-shaped opacities in the anterior and posterior subcapsular zones. They were more densely distributed toward the equator of each lens (coronary). Visual acuity was 6/6 in each eye.

CASE 61.—J. F., a woman aged 39.

A few grayish, punctate opacities were seen in the anterior and posterior cortices of the lens of each eye. Visual acuity was 6/6 in each eye.

CASE 62.—R. P., a youth aged 15.

A number of fine, grayish, dotlike opacities lay immediately behind the anterior capsule, and another, smaller group, just in front of the posterior capsule, of each eye, situated axially. Visual acuity was 6/5 in the right eye and 6/6 in the left eye.

CASE 70.—P. R., a woman aged 19.

A few fine white opacities lay in the anterior and posterior outer zones of the lens of the right eye. The same kind and arrangement of opacities were seen in the left eye, but with several yellowish and iridescent deposits and a vacuole of moderate size, all subcapsular, in the posterior zone. Visual acuity was 6/6 in each eye.

CASE 77.—R. B., a youth aged 17.

Two tiny, dotlike opacities were found in the posterior adult nucleus of each eye. Visual acuity was 6/6 in each eye.

CASE 78.—S. T., a girl aged 16.

There were several tiny grayish opacities in the posterior zone of the adult nucleus in the left eye. Visual acuity was 6/6 in each eye.

CASE 81.—E. B., a girl aged 16.

Several tiny whitish, dotlike opacities were seen in the outer layer of the posterior part of the adult nucleus in the left eye. Visual acuity was 6/8 in each eye.

CASE 82.—D. B., a woman aged 19.

A few tiny white, dotlike opacities were seen in the posterior cortex of each eye. Visual acuity was 6/6 in each eye.

CASE 83.—J. S., a man aged 25.

A few dirty white dots lay in the anterior and posterior portions of the adult nucleus of each eye, around the axillary zone, becoming typically characteristic of coronary opacities toward the periphery. Visual acuity was 6/6 in each eye.

CASE 85.—I. R., a youth aged 16.

A few punctate opacities were seen in the anterior cortex of the right eye. Visual acuity was 6/6 in each eye.

CASE 91.—M. T., a woman aged 21.

A few tiny white, dotlike opacities were seen in the posterior cortex of the lens in each eye. Visual acuity was 6/6 in each eye.

CASE 95.—D. G., a youth aged 17.

There was one white punctate opacity in the anterior cortex of the right eye. Visual acuity was 6/6 in each eye.

Of the patients with atopic dermatitis, acquired lenticular opacities of some kind were found in 45 (22.5 per cent) of all eyes and in 26 per cent of all patients—in the anterior portion of the lens in 5 eyes, in the posterior portion in 18 eyes and in both anterior and posterior portions in 22 eyes. Of the males 11 (30.5 per cent), and of the females 15 (23.4 per cent), were affected. The opacities were bilateral in 19 patients (73 per cent) and unilateral in 7 (26.9 per cent). The youngest was a girl aged 10, with bilateral opacities. The youngest male patient was 13 years of age, with bilateral opacities. The average age of all patients with opacities was 20.9 years.

COMMENT

From a comparison of the two groups of patients, it would seem that lenticular opacities on the whole are not found more frequently in patients with atopic dermatitis than in others, but in not 1 of the nonatopic group did we find a grossly demonstrable acquired cataract or one that could be considered potentially progressive, with the possible exception of patient 99.

On the other hand, in 8 patients (cases 1, 6, 9, 18, 24, 29, 32 and 70) of 100 with atopic dermatitis we have found a certain picture of cataracta complicata in some stage of development.

From our observation in this series of cases and in others we have seen, we should say that the cataract associated with and part of atopic dermatitis is characteristic. It nearly always appears first in the neighborhood of the pole immediately in front of the posterior capsule. It begins with one or two transparent globules or flattened vacuoles, a few tiny white or yellowish opacities and sometimes an iridescent crystal. These multiply, enlarge and coalesce until there is a mass of whitish, yellowish, transparent, translucent and opaque bodies of various shapes and sizes. It soon assumes a thin, but dense, irregularly translucent, generally yellow, disciform or rosette appearance and lies just in front of and parallel to the posterior capsule. It grows forward and peripherally, but mostly toward the equator. At the same time, or soon after, a process similar to that just described takes place in the anterior subcapsular zone of the lens.

At some stage in the development of atopic cataract a dense bluish, pearly white, plaquelike opacity is sometimes found just under the anterior capsule around the pole. Usually it is irregularly round, with scalloped or crenated edges and with extensions in the form of radiating solid or dotted lines toward the equator and the back of the lens. Sometimes the capsule over this so-called shield-shaped opacity is wrinkled, and sometimes it is elevated; but we agree thoroughly with Beetham that the opacity is entirely cortical and should not be called anterior polar or anterior capsular.

If, and as, the cataract continues to grow, the lens, as it becomes more and more involved, acquires a general relucency and finally reaches a stage which is in all respects like the mature cortical, senile type.

The average age of the patients with atopic cataracts in our series was 23.3 years, the youngest being 18 years old. Sack,[8] in a tabulated summary of 61 cases (33 American) reported prior to his own case (1947), gave the average age at which cataract developed as 25 years. This included 1 patient 49 years old. The average age of patients reported in the American literature, including the 49 year old patient, was 22 years. The youngest patient on record is the infant reported by Beetham,[1] and the next youngest, the 14 year old boy reported in the same series.

In our series, the cataract was bilateral in 5 patients and unilateral in 3. Of all the cases reviewed by Sack the cataract was unilateral in 8 and bilateral in 50, and in 3 the laterality was not given. All the cases of unilateral cataract were found in the American reports.

Of our patients 5 were females and 3 males. In Sack's tabulation of 61 patients 27 were females and 34 males. In the American reports the females predominate by 18 to 15. These data must be weighed by the fact that in our series of 100 consecutive patients there were 64 females and 36 males. On the basis of these figures, we might say that cataract occurs in 8.33 per cent of the males and in 7.7 per cent of the females with atopic dermatitis. We can find no comparable data in the literature.

SUMMARY

The eyes of 100 patients with atopic dermatitis were examined biomicroscopically and the findings compared with those of 100 patients with no evidence of local or general disease which might contribute to cataract.

Cataract characteristic of atopic dermatitis was found in 8 of 100 patients with atopic dermatitis.

The characteristic atopic cataract is described.

ABSTRACT OF DISCUSSION

Dr. William P. Beetham, Boston: Minute, unimportant acquired lenticular opacities are frequently seen. In the detailed survey of diabetic patients which Dr. J. Herbert Waite and I reported (*New England J. Med.* **212**:367; 429, 1935) in which approximately 1,000 eyes in the 20 to 40 year age group were studied with the biomicroscope and the widely dilated pupil, 80 per cent of the diabetic and 75 per cent of the nondiabetic patients had a clear cortex of the lens.

8. Sack, S. S.: Atopic Cataract, Ann. Allergy **5**:353, 1947.

This observation corroborates what the authors found in their run-of-the-office patients of the same age group; that is, 24 per cent of the eyes so examined had these relatively unimportant, acquired lenticular opacities.

Brunsting, in 1936, reported 101 cases of atopic dermatitis, and included in his group were 10 with cataract. The average age of 22 years in his series corresponds to the average age of 23 years in the present series and to the average age of 21 years for the 10 cases of cataract with atopic dermatitis which I reported in 1940, a condition for which I chose the name atopic cataract. The incidence of cataract of 10 per cent in Brunsting's series compares favorably with the 8 per cent incidence in a similar series of 100 cases in the Cowan and Klauder series.

Dr. Harriet D. James, one of the allergists at the Lahey Clinic, in Boston, reported to me a few days ago that she had picked 59 case records of atopic dermatitis at random and that in this group there was only 1 case with cataract. She felt, therefore, that the incidence in her group was somewhat less than that of the authors, possibly 2 or 3 per cent. It is possible that this incidence would have been higher if her cases had been studied in detail ophthalmoscopically.

I am perfectly willing to accept the sequence of events regarding the lenticular changes as described by Drs. Cowan and Klauder—the posterior, cortical, subcapsular changes occurring first, later the anterior, subcapsular changes, and still later, in some cases but not in all, the plaque or shield opacity, with its radiations and pseudopodia beneath the anterior capsule in the pupillary area. This plaque opacity is interesting to me, as I have rarely seen it except in the cataract associated with atopic dermatitis (1 slide from Vogt's "Atlas of Slit Lamp Microscopy of the Living Eye"; 3 slides, artist's drawings of cataract plaques; 1 kodachrome,* atopic cataract).

An amazing aspect of the authors' study is the unilateral involvement in one third of the cases; for this there is no explanation.

My interest in this subject originated with the case of a 14 week old infant, which I reported in 1940. This baby was admitted to the Massachusetts Eye and Ear Infirmary with a severe scaling, oozing eczema of the face, arms, legs and upper portion of the body, present since a few weeks after birth. The cataracts had developed after birth and at operation, when the child was 14 weeks old, were the typical, dense, opaque type of opacity in each eye. Quite possibly this case does not belong in this group, as the average age of cataract formation has been definitely set in the literature, and by the present authors, as between 20 and 25 years.

Intracapsular extraction is rarely performed in patients of this age group; nevertheless, in 2 of the 10 cases which I reported intracapsular extraction was performed. The cataracts so extracted were reported by the late Dr. Theodore L. Terry to have a normal capsule on histologic examination, although he had insisted prior to cataract extraction that the plaque opacity was a capsular, and not a cortical change.

Dr. Arthur Alexander Knapp, New York: In a previous publication I pointed out that according to the strict interpretation of the definition, that is, that cataract is any opacity in the lens, every one, infant and man alike, has cataract. This fact is readily demonstrated

by examination with the corneal biomicroscope. According to the more widely accepted definition, however, that is, an opacity of the lens causing loss of vision, relatively few persons are afflicted.

The authors, in their discussion of atopic cataract, pose an interesting problem: the allergic etiology of cataract. On the basis of reported research, the following questions are raised: The probable underlying pathologic condition of axial myopia is an exudative process in the fibrous tunic, a diffuse edema of the cornea and sclera. This results in weakening of the envelope. Frequently an allergic conjunctivitis accompanies myopia, and often there are other systemic manifestations of allergy, including cutaneous lesions. In the light of these findings, then, may not myopia be an allergic reaction of the eye? In support of this possibility is the fact that the myopia, the allergic conjunctivitis and the cutaneous lesions may be benefited by the administration of adequate doses of vitamin D and calcium. The cornea and sclera may shrink. It is well known that cataract, likewise an entity arising from excessive water intake, sometimes complicates axial myopia, or myopia without any lesion of the fundus. May not this type of cataract be allergic in origin? In truth, may not all cataracts have an allergic basis? For a few patients with early lenticular changes and mild to moderate loss of vision, I have prescribed sufficient vitamin D and ample calcium. There was suggestive improvement, but too few persons were observed and those over too short a time.

It would be interesting, therefore, in the light of this reported work, to learn whether the authors had treated any of their patients with atopic cataract with adequate doses of both vitamin D and calcium and, if so, to hear of their results.

Dr. Alfred Cowan, Philadelphia: I merely wish to thank Dr. Beetham and Dr. Knapp for their discussion, and to say that we have not used calcium or any vitamins in treatment of these patients.

A CONTRIBUTION TO KERATOPLASTY

K. LINDNER, M.D.
VIENNA, AUSTRIA

FLAWLESS excision of the cornea in the donor's and in the recipient's eye is of utmost importance to the final outcome of a partial penetrating corneal transplantation. Accurate performance of this part of the operation presents the main difficulty in an otherwise simple surgical procedure. Exact trephining of the donor's cornea can be achieved more easily because no special caution must be observed with respect to deeper structures of the eye. This is in contrast to the procedure on the patient's eye in which the technic of trephining must be carefully guarded because of the danger of injuring the iris, and particularly the lens. Generally it is advisable to discontinue the use of the trephine as soon as aqueous humor starts to escape and to complete excision by severing the remaining bridges of tissue with a pair of fine scissors. Most surgeons now prefer the hand trephine and believe that the risk of using the electrically or mechanically driven instrument is greater. The decisive points of the technic lie in placing the hand trephine on the cornea in perfect position and trephining with lightning speed so as to finish the trephination before the anterior chamber is totally evacuated. The use of Franceschetti's adjustable hand trephine with inner piston proved to be of great advantage.[1] This instrument prevents the sudden outflow of aqueous humor often experienced with the old models, and the danger to the lens is diminished by a device which regulates the height of the trephine crown. Nevertheless, it would be hazardous, even with this trephine, to continue the actual cutting for a moment after the aqueous humor begins to ooze out, especially if the anterior chamber is shallow. For this reason, broad bridges of tissue are often left even in eyes with corneas of equal thickness. These must be divided with scissors. Some of the later complications which result from an imperfect trephining procedure on the patient's eye are anterior synechias, improper position of the transplanted graft or late restoration of the anterior chamber, with subsequently developing rise in tension

From the Second Eye Department, University of Vienna.

1. The trephine is manufactured by E. Grieshaber, Schaffhausen, Switzerland.

In order to reduce the difficulties of this phase in the operation, I have used for some time a technic which consists principally of injecting Ringer's solution into the anterior chamber during the trephining procedure, provided that the anterior chamber is visible. The very sharp needle on a 2 cc. Pravaz syringe is introduced horizontally from the temporal side into the lowest segment of the anterior chamber so that the point of the needle is placed at 6 o'clock in front of the iris. While the trephine is being used, the assistant must keep the anterior chamber under a certain pressure, which causes an increase in its depth. When the aqueous begins to escape through the trephine wound, it will be partly replaced with Ringer's solution. Thus, additional time is gained for continuing the trephining without endangering the lens.

Thrusting of the needle through the cornea is not always easy. The usual needles are not sufficiently sharp. Mr. Grieshaber has designed a lancet needle which penetrates the cornea more smoothly. Its caliber is selected to guarantee sufficiently rapid replacement of the escaping aqueous humor. The penetration of a usual needle may be facilitated by partial incision of the cornea with the keratome and insertion of the needle in the wound.[2] However, the necessarily short needle track causes leakage of aqueous humor along the needle. This leakage can be avoided by making a long, oblique needle track that passes through the entire thickness of the cornea. Obviously, it is necessary that the assistant hold the needle carefully in a steady position. Accidental injury of the lens with the point of the needle can thereby be averted.

In 1 instance the needle detached a fine membrane from the posterior surface of the cornea, which could be removed *in toto* after completion of trephining. It consisted of a thin layer of connective tissue which was attached to the cornea. The transplant in this eye became turbid, but this may have occurred without the complication mentioned.

The injection of Ringer's solution with a certain pressure leads to deepening of the anterior chamber. It may become very deep when more pressure is exerted, and the cornea of a young patient may be slightly stretched. After removal of the corneal flap, the opening is somewhat smaller than the corresponding transplant. The difference is very moderate, definitely less than 0.1 mm. Franceschetti recommended formerly the use of two trephines with a difference in

2. I described this technic for the injection of 10 per cent trichloroacetic acid (thirty seconds) in coagulation therapy of cysts of the iris. Linder, K.: Klin. Monatsbl. f. Augenh. **102**:589, 1939.

diameter of 0.1 mm. and chose grafts about 0.1 mm. greater than the opening. Later he changed the technic by employing the instrument with the greater diameter on the eye of the patient. In my series, no difficulties were encountered in placing the transplant in the patient's cornea.

The procedure described can be utilized also in cataract operations on eyes with a very shallow anterior chamber. Originally I used it for the Sato operation for keratoconus. The operation can be carried out without strain and according to plan when the anterior chamber is kept deep. It is not possible to accomplish this without the described technical modification.

Correspondence

AUREOMYCIN IN TREATMENT OF VIRUS DISEASES

To the Editor:—Communications from various authors have emphasized the possibility of treating virus diseases with aureomycin. Dendritic keratitis is a case in point. For this reason, when I was faced with a case of conjunctivitis of supposed Newcastle (Philippine fowl) disease aureomycin was used.

The patient, a poultry farmer aged 50, had an epidemic of Newcastle disease among his chickens. Two days prior to his consulting me, he had had onset of severe pain, burning and redness of both eyes. There were no associated systemic complaints. Physical examination revealed considerable injection of both the bulbar and the palpebral conjunctiva. There was no evidence of iritis. The pupils reacted to light, and funduscopic examination revealed nothing abnormal. A smear of the secretion revealed a predominance of lymphocytes and no organisms. Antistin® (2-[N-phenyl-N-benzylaminoethyl]-imidazoline) ophthalmic, which had been given because of the possibility of an allergic origin, was discontinued. No new effect having been noted in twenty-four hours, aureomycin was then prescribed locally only. There was no parenteral therapy. The preparation used was "aureomycin hydrochloride ophthalmic" (Lederle), which contains 25 mg. and is diluted with 5 cc. of distilled water. This solution must be made up fresh every two days and should be refrigerated when in use. Instillation of 1 or 2 drops in each eye every two to three hours is prescribed—in this case every three hours. Relief was almost immediate, and within twelve hours the patient's condition had improved remarkably. A neighboring poultry farmer in whom unilateral conjunctivitis developed, and who was not seen by me, also responded in a short time to treatment with the drug.

While the conjunctivitis of Newcastle disease is not mentioned in the standard textbooks, so far as I can find, it is apparently a well recognized entity among persons who work experimentally with the virus. It is suggested that it be considered a possible etiologic agent in the case of poultry farmers and that the exhibition of aureomycin is apparently curative.

GEORGE A. SHEEHAN JR., M.D., Red Bank, N. J.
27 Irving Place.

News and Notes

EDITED BY DR. W. L. BENEDICT

GENERAL NEWS

Ophthalmology and Otolaryngology.—The next meeting of the Central Illinois Society of Ophthalmology and Otolaryngology will be held at the Illinois Hotel, Bloomington, Ill. on April 21, 22 and 23. Dr. A. E. Braley, of New York, will give several lectures on diseases of the eye; Dr. Louis Clerf, Philadelphia, will discuss laryngeal diseases; Dr. Louis Ostrom, of Rock Island, Ill., and Dr. H. Middleton, of Alton, Ill., will also give papers.

Annual Examination for Technicians, American Orthoptic Council.—The annual examination of orthoptic technicians by the American Orthoptic Council will be conducted in September and October 1950. The written examination will be nonassembled and will take place on Thursday, September 7, in certain assigned cities and offices and will be proctored by designated ophthalmologists. The oral and practical examinations will be on Saturday, October 7, in Chicago, just preceding the meeting of the American Association of Orthoptic Technicians.

Application for examination will be received by the office of the secretary of the American Orthoptic Council, Dr. Frank D. Costenbader, 1605 22d Street, Northwest, Washington 8, D. C., and must be accompanied with the examination fee of $25. Applications will not be accepted after July 1, 1950.

Annual Meeting of Pennsylvania Academy of Ophthalmology and Otolaryngology.—The annual meeting of the Pennsylvania Academy of Ophthalmology and Otolaryngology will be held May 12 to 14 at the Bedford Springs Hotel, Bedford, Pa. Among the speakers who will present papers at this meeting will be Drs. Edward H. Campbell, Frank D. Costenbader, Karl M. Houser, Raymond E. Jordan, John E. L. Keyes, John A. Kolmer, Francis L. Lederer, Irving H. Leopold, Maurice Saltzman, Richard G. Scobee, Edmund B. Spaeth and Frank B. Walsh.

In addition to the formal presentations, twelve study clubs will be conducted, to run concomitantly with the scientific sessions. Topics to be discussed will be "Refraction Difficulties in Presbyopia" and "Common Office Procedures in Otorhinolaryngology."

UNIVERSITY NEWS

Grant to Department of Ophthalmology, University of Toronto.—The Department of Ophthalmology of the University of Toronto has received a grant from the Ontario Provincial Department of Health through funds provided by federal grant for research work on the

prevention of blindness from glaucoma. This work will be done under the direction of Dr. T. H. Hodgson in the Banting Institute, Toronto General Hospital and other university teaching hospitals in Toronto. The initial grant was $8,200. It is proposed that the research work will extend over three to five years.

CORRECTION

In the article by L. W. Chacko, M.B., entitled "Relation of Color Sensitivity in the Visual Field to the Laminar Pattern in the Lateral Geniculate Body," which appeared in the October 1949 issue of the ARCHIVES, pages 403-409, the address (page 409) should be "Christian Medical College, Vellore, South India."

Abstracts from Current Literature

EDITED BY DR. WILLIAM ZENTMAYER

Blindness

SIGHT RESTORATION IN A SCHOOL FOR THE BLIND. P. DORMAN, Am. J. Ophth. **32:** 433 (March) 1949.

Dorman discusses restoration of sight under the heading of prenatal care, actual visual improvement and psychologic adjustment. The article does not lend itself to abstraction.

W. S. REESE.

Congenital Anomalies

PERSISTENT HYALOID ARTERY WITH ABSENCE OF RETINAL VESSELS. R. BERNOULLI, Ophthalmologica **117:** 169 (March) 1949.

In a 7 year old boy, a large reddish yellow band was seen to extend from the region of the disk to the posterior pole of the lens. The diagnosis was persistent hyaloid artery surrounded by a thickened glial sheath with many small vessels on the surface. There was complete absence of retinal vessels. The choroidal circulation was clearly visible. The combined occurrence of persistence of the hyaloid artery and absence of retinal vessels has been reported but once before (Magnus 1927). The author attempts to explain the genesis of this maldevelopment.

H. P. KIRBER.

BILATERAL ANIRIDIA WITH PTOSIS AND EMBRYOTOXON: GONIOSCOPIC EXAMINATION. ESTEBAN ADROGUE and JORGE A. WOLF, Arch. oftal. Buenos Aires **23:** 141 (July-Aug.) 1948.

A detailed case history is presented, the summary of which follows: A married woman aged 28 had marked ptosis of the upper lid and bilateral enophthalmos, the retraction measuring 9 mm. Ocular movements were normal except for slight limitation for lateral and vertical movements. The periphery of the cornea showed turbidity of the superficial layers, the opacity varying in width from 2 to 4 mm. and extending to the limbus. Isolated vessels were noted in the peripheral part of this opacity. The cornea was small, being 9.5 mm. in diameter in each eye. The depth of the anterior chamber was normal. Examination in ordinary light showed an apparent total absence of the iris and nystagmus. The lens presented anterior and posterior cataracts and coronary opacities in the periphery. Visual acuity in each eye was limited to counting finger at 2 meters. The findings on gonioscopic examination are given in detail. The authors present general considerations on aniridia.

M. E. ALVARO.

Cornea and Sclera

ECZEMATOUS KERATITIS AND ARIBOFLAVINOSIS. H. J. STERN and J. LANDAU, Am. J. Ophth. **31**: 1619 (Dec.) 1948.

Stern and Landau report that riboflavin has a marked therapeutic effect on eczematous keratitis. They feel that ariboflavinosis is the essential basic condition of the disease.

W. S. REESE.

KERATOPLASTY. O. S. LEE JR. and L. ALLEN, Am. J. Ophth. *32*: 71 (Jan.) 1949.

Lee and Allen give this preliminary report on an ingenious instrument to be used in cutting corneal grafts in keratoplasty. A number of transparent grafts obtained in rabbits with this instrument are pictured.

W. S. REESE.

SOME UNUSUAL CASES OF SJÖGREN'S SYNDROME. H. COVERDALE, Brit. J. Ophth. *32*: *669* (Sept.) 1948.

Coverdale reports 5 cases of keratitis sicca. The first case was that of a man aged 68 who had been in the habit of sitting with his eyes closed. After onset of hemiplegia he was found to have typical filamentous keratitis. The second case was that of a woman aged 36, the daughter of the first patient. She had a lifelong history of dry eyes; it is probable that the condition was congenital. There were evidences of dysfunction of the pituitary gland. The third and fourth cases were those of a woman and her daughter, the latter having pulmonary tuberculosis. The mother was 58. In the fifth case the ocular condition seemed to arise from a fracture of the base of the skull. In speculating on the cause of the syndrome, the author states that allowance must be made for the possibility that the pathologic process began long before the first complaint of symptoms. The doubtful positive reaction to the Wassermann test in case 2 and the tuberculosis in case 4 suggest infection as a causative factor, but it is more reasonable to suspect the presence of a congenital defect, which may be made manifest at any period of life by any precipitating circumstance.

W. ZENTMAYER.

HISTOLOGIC EXAMINATION OF A TRANSPARENT CORNEAL GRAFT: BEHAVIOR OF THE NERVES. A. FRANCESCHETTI and J. BABEL, Ann. d'ocul. **180**: 142 (March) 1947.

The authors had occasion to examine a clear corneal graft six years after the corneal transplant. There was considerable vascularization of the recipient cornea, but no large vessels were seen in the graft. Bowman's membrane was absent from the host cornea (because of the original infection), but was well preserved in the graft. The nerves were abundant in the host cornea. Only a few fine fibers were seen on the anterior and posterior surfaces of the graft. They appeared to parallel the vascularization, since only a few capillary loops were seen in the graft.

The authors conclude that the primitive structure of the graft is maintained, that some cellular elements pass from the host to the

transplant and that the innervation is secondary to the vascularization. The only nerves visible on microscopic examination of the graft were the subepithelial fibers. These have not been seen on histologic examination of opaque grafts. It may be that the presence of these fibers is a factor in whether the graft will remain clear. P. R. McDONALD.

HEREDITARY AND FAMILIAL MEGALOCORNEA. R. NATAF and P. FONTAN, Ann. d'ocul. **180:** 267 (May) 1947.

The authors report in detail a case of megalocornea occurring in a 20 year old soldier. The right cornea measured 16 mm. and the left 17 mm. in diameter. Both corneas showed an embryotoxon. There was a bilateral iridodonesis. The right lens was normal. The left lens presented an abnormality between 1 and 5 o'clock. The edge was thinned and irregular, like a sliver of ice. The zonular fibers were clearly visible; some of them floated freely and were not attached to the lens. Gonioscopic examination was not possible because no instrument was available for such a large cornea. In reviewing the family history, it was found that the maternal grandfather had megalocornea. He had had a bilateral cataract extraction at the age of 66. Of the patient's six brothers and sisters, his next oldest brother presented the same disorder.

The authors believe the dislocation of the lens is due to the zonular fibers failing to keep pace with the growth of the anterior segment. They rupture, and this is followed by a dislocation of the lens.

P. R. McDONALD.

PROCURING OF A GRAFT FOR KERATOPLASTY. M. AMSLER and F. VERREY, Arch. d'opht. **8:** 150 (Feb.) 1948.

The authors describe a method of procuring a corneal graft without producing any mutilation, at the same time obtaining a clear graft. During the excision and manipulation of the cornea, no instrument comes in contact with the portion which will be the graft. The part not used is submitted to histologic examination for comparison unless it is used for a second transplantation.

S. B. MARLOW.

Experimental Pathology

EXPERIMENTAL LENTICULAR OPACITIES PRODUCED BY MICROWAVE IRRADIATIONS. A. W. RICHARDSON, T. D. DUANE and H. M. HINES, Arch. Phys. Med. **29:** 765 (Dec.) 1948.

Richardson and his co-workers state that the development of cataract as the result of irradiation is not a new discovery, but investigators in the past have been concerned chiefly with the effects of infra-red, ultraviolet and roentgen irradiations. For a number of years short wave diathermy has been used extensively in treatment of disorders of the sinuses and have proved safe when used as prescribed. With the production of a new microwave generator which propagates 12.25 cm. waves, a new band of the electromagnetic spectrum has been offered for medical

therapy. The authors investigated both the immediate and the delayed effects of microwave irradiations on the eye. A direct single exposure of rabbit eyes to 12.25 cm. microwaves at a distance of 5 cm. for fifteen minutes with 100 watt power output resulted in the appearance of cataractous lenticular opacities after a delay of three to nine days. A series of repeated exposures of a smaller magnitude resulted in the development of cataractous lenticular opacities after a delay of two to forty-two days. Four rabbits given irradiations for seventeen to twenty minutes at a distance of 5 cm. revealed cataract formations immediately after the irradiations. Since other workers have shown that the microwave generator serves an adequate purpose in medical therapy by inducing increases in temperature in selected areas of the body, the findings in this report should not discourage its employment in those areas. Precaution should be taken in the future with regard to irradiations in the region of the face and orbit. J. A. M. A. (W. ZENTMAYER.)

BLOOD-VESSEL FORMATION IN THE CORNEA. F. W. CAMPBELL and I. C. MICHAELSON, Brit. J. Ophth. **33**: 248 (April) 1949.

The authors studied the phenomenon of vascularization in localized lesions of the cornea. A "standard lesion" was produced by applying a platinum wire cautery to the rabbit cornea for approximately two seconds. The cautery was kept at a uniform temperature throughout the experiment by supplying a constant voltage. The application was repeated daily at the same site, usually from ten to fourteen days. The lesion was about 1 mm. in diameter and involved the epithelium and the superficial two thirds of the substantia propria. The authors summarize their work as follows:

A method is described for producing a relatively standard corneal lesion in rabbits and for studying the resulting vascularization of the cornea. If the lesion is more than a certain critical distance from the limbus, no vascular response occurs. At less than this distance from the limbus, vascularization occurs, and the vascular area has the form of an isosceles triangle. If a series of "standard lesions" are placed at different distances from the limbus, but within the critical distance for that lesion, the distances between the sites of the lesions and the basal angles of the triangular vascular areas are fairly constant. The results suggest that the formation of new vessels in the cornea, in the circumstances described, involves a factor released by the lesion and diffusing from the site of that lesion. W. ZENTMAYER.

General

APPARENT ROTATION OF A FIXED TARGET ASSOCIATED WITH LINEAR ACCELERATION IN FLIGHT. B. CLARK and A. GRAYBIEL, Am. J. Ophth. **32**: 549 (April) 1949.

Clark and Graybiel found illusory effects similar to those observed in experiments on a human centrifuge in their investigations of a series of airplane accidents. These results show that linear acceleration and deceleration during flight have a influence on visual perception in the dark. Although the observed rotations were small, they were clearly defined and may be considered to be factors contributing to disorientation in pilots. W. S. REESE.

General Diseases

HARADA'S DISEASE. M. G. BRUNO and S. D. MCPHERSON JR., Am. J. Ophth. 32: 513 (April) 1949.

Bruno and McPherson report 4 cases of Harada's disease. They discuss the etiology and relation of Harada's disease to the Vogt-Koyanagi syndrome and sympathetic ophthalmia. It seems possible that there may be a common etiologic factor responsible for all three conditions.

W. S. REESE.

PAPILLOEDEMA IN EMPHYSEMA. THOMAS SIMPSON, Brit. M. J. 2: 639 (Oct. 2) 1948.

This is a report of papilledema occurring in 3 cases of emphysema. The literature is reviewed, and the author concludes that papilledema complicating emphysema results from an increase in the intracranial fluid pressure.

ARNOLD KNAPP.

EXPERIMENTAL STUDIES ON THE PATHOGENESIS AND TREATMENT OF OCULAR TUBERCULOSIS. A. C. WOODS, Brit. J. Ophth. 33: 197 (April) 1949.

This lengthy and important article is the inaugural address at the opening of the Institute of Ophthalmology, London.

After an introductory paragraph, in which the immediate objectives of these investigations are stated, the pathogenesis of ocular tuberculosis is dealt with under the headings of (1) influence of the number and virulence of organisms, (2) influence of hypersensitivity on the ocular lesion and (3) influence of immunity on the ocular lesion. The treatment of experimental ocular tuberculosis is discussed under the headings of the enhancement of immunity, the effect of desensitization on experimental ocular tuberculosis and the effect of chemotherapy and use of antibiotics on ocular tuberculosis.

The following summary is given:

Rich's law for the pathogenesis of tuberculous lesions appears to hold true in localized ocular tuberculosis. The factors governing the course and character of the lesion are the number and virulence of the infecting organisms, the degree of tissue hypersensitivity present and the amount of the resistance established by the host. These studies also offer an explanation for the relative cutaneous anergy often present in animals and man with inflammatory tuberculous lesions of the eye. This concept of the pathogenesis of a tuberculous lesion offers obvious points for therapeutic attack on the disease. The first of these is enhancement of immunity, and nothing specific has been done as yet to stimulate local resistance artificially. The second is removal of the fatal tissue hypersensitivity; this can usually be accomplished by the use of tuberculin as a desensitizing agent, and has a distinctly beneficial effect on the clinical course of the lesion. The third is the direct attack on the tubercle bacilli, and in streptomycin and promizole® (4,2'-diaminophenyl-5'-thiazole sulfone) combined one has a powerful weapon to this end. Doubtless

other, better antibiotics and sulfones will be found, but at present this combination appears the best available. The article is illustrated with numerous colored plates and photomicrographs. W. ZENTMAYER.

CATARACT ASSOCIATED WITH POIKILODERMA AND SCLERODERMA. A. FRANCESCHETTI and G. MAEDER, Ophthalmologica **171:** 196 (April-May) 1949.

Poikiloderma, or the syndrome of Rothmund, is a hereditary disease, of which about 20 cases are on record. It affects mainly girls at puberty, is characterized by abnormal pigmentation of the skin, telangiectasia and scarring, particularly of the face and forearms. Endocrine disturbances, such as genital hypoplasia, are frequent. Scleroderma, or the syndrome of Werner, is a similar disease. Forty-two cases are on record. It affects mainly males, starts at puberty and is characterized by cutaneous lesions of the lower extremities predominantly (trophic ulcers), hyperkeratosis of the hands and feet and abnormal distribution of hair. Both diseases manifest themselves in the eye by cataract formation. The author describes a number of cases he has seen and reviews several from the literature. He points out that the ophthalmologist is frequently the first to diagnose the disease. H. P. KIRBER.

VALUE OF PHLYCTENULAR KERATOCONJUNCTIVITIS IN EPIDEMIOLOGY OF TUBERCULOSIS. JUAN MANUEL VILA ORTIZ and JUSTO LOPEZ BONILLA, Arch. oftal. Buenos Aires **23:** 184 (July-Aug.) 1948.

The authors state that phlyctenular keratoconjunctivitis is a disease of a predominantly allergic nature. Its origin in the majority of cases is tuberculous, and it should be considered a manifestation of activity, immediate or latent, of a primary infection. A patient with phlyctenular keratoconjunctivitis should always be given a tuberculin test and a roentgenologic examination, not only the patient himself but also the members of his family, as in a high percentage of cases the source of infection can be found among the latter. The authors place special emphasis on this part of the examination. M. E. ALVARO.

CONGENITAL ECTOPIA OF THE LENS WITH SPHEROPHAKIA AND SHORT STATURE, ACCOMPANIED WITH PARALYSIS OF GAZE (MARCHESANI'S SYNDROME). W. STADLIN AND D. KLEIN, Ann. d'ocul. **181:** 692 (Nov.) 1948.

Ectopia lentis is frequently associated with other congenital defects, as in Marfan's syndrome. Arachnodactyly is characterized by increase in length, laxness of ligamentous structures and other congenital defects. Marchesani (1939) described another syndrome, characterized by brachydactyly, ectopia lentis and spherophakia. Patients with this syndrome have round heads and short, stalky limbs, and the motility of their joints is normal.

The authors describe a patient who presented the signs and symptoms of this syndrome, as well as supranuclear paralysis of gaze. The genealogy of the patient is presented. The parents were second cousins; the mother was short and stocky, and the father had very small hands and

feet. It is probable that the Marfan and the Marchesani syndrome differ only in that one shows hyperplastic and the other hypoplastic disturbances in the skeletal system. Schmid has linked the two conditions under the term "dysmorpho-dystrophia mesodermalis congenita."

P. R. McDonald.

Glaucoma

Newer Concepts in the Classification of the Glaucomas. H. S. Sugar, Am. J. Ophth. **32:** 425 (March) 1949.

Sugar presents a new classification of glaucoma based on clinical evidence. The classification of the glaucomas is arranged so as to include the same groupings into primary and secondary glaucoma which usage has made universal. Emphasis is placed on routine tonometry in all patients 40 years of age or over.

W. S. Reese.

Use of Tantalum Implants for Inducing a Permanent Hypotony in Rabbits' Eyes. M. Uribe Troncoso, Am. J. Ophth. **32:** 499 (April) 1949.

Troncoso found that tantalum is well tolerated by the rabbit eyes and may be kept in position a long time after cyclodialysis or trephining. Using a tantalum tube, he was able to produce hypotony, which in some rabbits lasted eight months.

W. S. Reese.

Treatment of Chronic Glaucoma with Nicotinic Acid. C. Monfette, Union méd. du Canada **77:** 1433 (Dec.) 1948.

Monfette treated with nicotinic acid 2 women, aged 55 and 56 respectively, who had chronic glaucoma. This vasodilator has been employed by Gallois, in France, for twelve years with satisfactory results in cases of glaucoma in which the intraocular pressure did not exceed 50 mm., particularly cases of simple chronic glaucoma in the early stage, in which the vascular lesions are not yet accentuated. Repeated vasodilator tests with intravenous doses of 2 to 3 mg. of the drug two or three times a week must precede the treatment. Each test is followed by tonometric readings every fifteen minutes for one hour; each period of tonometric determination is preceded by measurements of the central visual acuity. The dose was 1 mg. of nicotinic acid in 1 teaspoon of distilled water, 2 teaspoons (8 to 10 cc.) being given daily. In both patients vision was improved from 15/30 to 15/20, and tension was reduced from 26 to 20 mg. in one patient and from 25 to 19 in the other. Headache disappeared, as did the clouds before the patients' eyes. Although 2 cases do not form a sufficient basis for any conclusions, the results of treatment seem to support Gallois'.

J. A. M. A. (W. Zentmayer).

Glaucoma and the Excavation of the Papilla. D. Díaz Domínguez, Arch. Soc. oftal. hispano-am. **8:** 1219 (Dec.) 1948.

Díaz Domínguez discusses the relation of ocular hypertension and changes in the excavation of the optic nerve head and supports his opinions with personal observations. He arrives at the following con-

clusions. 1. The changes in shape and depth of the papillary excavation are not in direct proportion to the ocular hypertension. 2. The absence of glaucomatous cupping in cases of prolonged hypertension is probably caused by diminished rigidity of the coats of the eye. 3. On the other hand, an increase in the depth of the physiologic excavation is related to an increase in the rigidity of the coverings of the globe and to sclerosis of the blood vessels of the circle of Haller. 4. In almost all cases of glaucoma without hypertension or of pseudoglaucoma, the condition is true glaucoma with discrete or intermittent hypertensions. 5. True simple glaucoma is a senile condition, more so than is cataract or senile macular degenerations.

H. F. Carrasquillo.

Clinical Study of Glaucoma. W. J. Kapuscinski, Ann. d'ocul. **181**: 542 (Sept.) 1948.

The author refers to the various provocative tests for the diagnosis of glaucoma. The water-drinking, caffeine and venous compression tests, as well as galvanic stimulation of the cervical ganglion, are based on the theory of disturbing the vasomotor balance within the eye. The darkness test causes the pupil to dilate, thus mechanically narrowing the angle of the anterior chamber. In 41 cases in which these tests were employed the results were of little value when the diagnosis was doubtful.

Dark adaptation was impaired in all patients with chronic simple glaucoma, but there was no correlation between the results and the patients' symptoms of night blindness. The impaired dark adaptation may be ascribed to a disturbance of the hypothalamus which causes a change in the melanophore hormone.

The author cites several cases of juvenile glaucoma in which pilocarpine raised and atropine lowered the tension. He concludes that juvenile glaucoma does not have the same etiologic basis as glaucoma in adults.

After a discussion of glaucoma without hypertension, the author concludes by agreeing with Magitot that hypertension is a symptom and that glaucoma is not synonymous with increased intraocular pressure.

P. R. McDonald.

Orbit, Eyeball and Accessory Sinuses

Association of Malignant Exophthalmos, Increased Basal Metabolism and Paralysis Agitans and Their Relation to Thyrotoxicosis. L. Paufique and P. Guinet, Ann. d'ocul. **181**: 665 (Nov.) 1948.

The authors report the case of a man aged 61 with hypertension, paralysis agitans, a basal metabolic rate of + 79 to + 100 per cent and malignant exophthalmos. The clinical features, pathologic changes and treatment of malignant exophthalmos are reviewed.

The coexistence of the various symptoms suggests that there must be a disturbance in the central nervous system. Treatment, therefore, is directed to inhibiting the thyrotoxic factors by medication or by roentgen therapy directed at the pituitary gland.

P. R. McDonald.

Parasites

OCULAR CYSTICERCOSIS. L. JUNIOR, Am. J. Ophth. **32**: 523 (April) 1949.

Junior reports the observations of the ophthalmologists and pathologist of the Instituto Penido Burnier on 111 patients with ocular cysticerci. He reviews the history, etiology, pathogenesis, diagnosis and treatment.

W. S. REESE.

Refraction and Accommodation

TISSUE THERAPY IN COMPLICATED MYOPIA. R. DE SAINT-MARTIN, Ann. d'ocul. **181**: 577 (Oct.) 1948.

The author has used tissue therapy, as suggested by Filatov, in cases of retinitis pigmentosa, severe iridocyclitis, sympathetic ophthalmia and complicated myopia. In many instances the patients were most enthusiastic, although in some cases the symptomatic improvement was not verified by improvement in visual acuity and other objective criteria.

The technic of preparation of the extract and its mode of administration are described in detail. The treatment was given in 36 cases of complicated myopia, and the results in 30 are discussed in detail. Of the 30 cases, there was remarkable improvement in 8, appreciable improvement in 14, doubtful improvement in 6 and failure in 2.

Three cases of high myopia with retinal detachments which had not responded to surgical treatment are also reported. The condition responded well to tissue therapy with flattening of the retina.

P. R. MCDONALD.

Retina and Optic Nerve

SURGICAL TREATMENT OF RETINAL DETACHMENT WITHOUT RETINAL TEAR. A. DE ROETTH SR., Am. J. Ophth. **32**: 55 (Jan.) 1949.

De Roetth reports good results obtained in 3 of 7 cases of retinal detachment with poor prognoses by the use of a metal drain designed to drain off the subretinal fluid for several days. Surface diathermy and injection of air into the anterior chamber are also used.

W. S. REESE.

SURGICAL TREATMENT OF RETINAL DETACHMENT. J. P. VERDAGUER, Am. J. Ophth. **32**: 63 (Jan.) 1949.

Verdaguer describes his method of treating retinal detachments. He believes that operation should be performed in all cases of this lesion, as the prognosis is otherwise hopeless.

W. S. REESE.

SCLERAL STAPHYLOMA AND RETINAL DETACHMENT. D. VAIL, Am. J. Ophth. **32**: 1111 (Aug.) 1949.

Vail discusses scleral staphyloma and retinal detachment. He concludes that retinal detachment may occur subsequent to a scleral staphyloma in the affected area.

W. S. REESE.

RETINAL HOLES WITHOUT DETACHMENT. E. WEBER, Ophthalmologica **117**: 263 (April-May) 1949.

Multiple small round retinal holes in the lower sector of the periphery of the retina were noticed in a frequency of 2 per thousand patients in private practice. No classification as to age, refraction or pathology of the fundus is given. The holes are frequently bilateral, and surgical treatment should not be undertaken. In the discussion of this paper, it was pointed out by Girardet that in perfectly healthy eyes thinning of the retina in the periphery can simulate a true hole and that ophthalmoscopy with intense illumination by special lamps is recommended in the differential diagnosis. Goldmann confirmed the diagnosis of true holes in 1 of the cases described by means of the contact lens and slit lamp with the binocular ophthalmoscope.

H. P. KIRBER.

CEREBRAL AND RETINAL ANGIOPATHY. A. HUBER, Ophthalmologica **117**: 265 (April-May) 1949.

Sclerosis of the retinal arteries, even of a severe degree, does not permit the assumption of sclerosis of the cerebral arteries. This has been demonstrated by Rintelen. The author is of the opinion that the same holds true for hypertensive changes. In old age, however, the perisclerosis of the adventitial coat of the retinal arteries corresponds to the same changes present in the arterioles of the brain. Aneurysms of the cerebral arteries rarely have a counterpart in the retinal vessels. In only 20 per cent of cases of the von Hippel–Lindau syndrome, are there angiomas of the cerebral vessels. Two cases of thromboangiitis obliterans are described in which optic nerve atrophy, obliteration of retinal arteries and thrombosis of the internal carotid artery and its branches were present. This disease is a better example of the close relation of retinal and cerebral vessels than arteriosclerosis, hypertension and angiomatosis.

H. P. KIRBER.

Sympathetic Ophthalmia

NERVOUS AND MENTAL SIGNS ASSOCIATED WITH SYMPATHETIC OPHTHALMITIS. P. TOULANT and A-M. LARMONDE, Bull. Soc. d'opht. de Paris, October 1948, p. 534.

Recent studies on sympathetic ophthalmia in 3 patients have demonstrated lesions in the meninges. The patients were peculiarly taciturn, hostile and irritable. A review of other case reports in the literature have convinced the authors that lesions of the central nervous system may readily explain the cause in most cases of sympathetic ophthalmia.

L. L. MAYER.

Society Transactions

EDITED BY DR. W. L. BENEDICT

COLLEGE OF PHYSICIANS OF PHILADELPHIA, SECTION ON OPHTHALMOLOGY

Alfred Cowan, M.D., Acting Chairman

M. Luther Kauffman, M.D., Clerk

March 18, 1948

Indications and Results in Keratoplasty. DR. HAROLD G. SCHEIE.

The results of corneal transplantations performed on 22 eyes at the Hospital of the University of Pennsylvania were discussed. Nineteen of the eyes were followed through convalescence, and the statistics presented were based on these eyes, although it was realized that the number was too small to be of statistical significance. The eyes were classified according to Castroviejo's grouping, from group 1, with the most favorable prognosis, to group 4, with the least favorable prognosis. Three criteria were used in judging the success or failure of the operation: (1) clarity of the graft, (2) improvement in visual acuity and (3) benefit to the patient.

Six patients were of group 1, the condition including those with a central corneal scar resulting from old keratitis, keratoconus and central scars of interstitial keratitis. All the patients in group 1 obtained clear grafts and improved visual acuity, which was striking in 3 patients. When improvement did not result, amblyopia ex anopsia or central scotoma was the explanation. The criterion of actual benefit to the patient derived from the operation offers an even more critical, and possibly more practical, way of evaluating corneal transplantation. In spite of clear grafts and visual improvement in all 6 patients, only 4 used the eye operated on, and thus derived benefit from the procedure. The astigmatic errors varied from 2 to 5 D.

Only 3 of the 4 patients in group 2 have completed their convalescence. Two of these 3 patients have clear grafts. All have rather remarkable improvement in vision, but only 2 of the 3 have obtained real benefit from the operation, the third not using the eye with the transplant.

Only 2 patients comprised group 3. The first patient had had recurrent corneal ulceration with severe discomfort for three years. He had reached the point where he preferred enucleation of the eye to further discomfort. The involved area of the cornea was central. A corneal transplantation was done; the graft has remained clear and has made him more comfortable. Vision, however, has not improved, because of a preexisting complicated cataract. He should have a good eye after the extraction. The other patient had central scarring from old keratitis, but the lens had been subluxated by a former injury and was cataractous.

A transplantation was done in the hope of giving him a clear cornea before cataract extraction, but the graft became opaque and he has been made definitely worse by the operation.

Group 4 included 8 patients with serious corneal conditions, such as epithelial dystrophy, severe corneal degeneration as a result of interstitial keratitis, extensive mustard gas burns of the cornea and recurrent ulcerative keratitis with calcareous degeneration (1 case). A clear transplant has been obtained in only 1 patient and significantly improved vision in only 3. However, 4 of the 8 patients have shown dramatic improvement, either visual or through alleviation of symptoms. The most dramatic benefit was that of a soldier with severe mustard gas burns of both corneas. Only 1 patient was made worse by the grafting. One patient had a prolapse of the iris, with eventual loss of his eye.

Taken as a whole, visual improvement was obtained in 65 per cent of patients; in 50 per cent the grafts remained clear. Fifty-six per cent of the patients were benefited by the operation; 31 per cent were unimproved, and 10 per cent were made worse, although the loss is difficult to assess, since their vision had been limited to perception of hand movements and light, respectively, before operation. Since 8 of the patients were in group 4, the over-all figures are not discouraging.

The indications for corneal transplantation were summarized as follows: 1. The favorable conditions of groups 1 and 2 are preferred, but when a patient has a chance of visual or symptomatic gain and nothing to lose corneal transplantation can justifiably be done. 2. Vision should be less than 6/60. 3. Hesitation is advised in cases of unilateral involvement. 4. A one-eyed patient should be operated on only if his eyesight is of no practical value to him.

DISCUSSION

Dr. James S. Shipman: The picture of keratoplasty which Dr. Scheie has given is very different from that which too often is given the public. It is regrettable that the subject cannot be presented to the public, through the newspapers, in its true light.

The actual cases as presented here are evidence of the excellent technic used by Dr. Scheie. Indeed, they give convincing evidence for use of the circular transplant.

In 1 of the cases presented by Dr. Scheie I did a corneal transplantation about six years ago. At that time surgeons were using the double-bladed knife of Castroviejo and obtaining a square graft. In this case everything went well until about a week after operation, when secondary glaucoma developed. This was eventually controlled with miotics. Dr. Scheie encountered this complication in only 1 of his series of 20 cases. In this case very severe interstitial keratitis had been present. A short while after operation there developed a striking increase in, and overfilling of, old corneal vessels. As a result, the corneal graft went on to complete opacification, and the cornea was as opaque as it was before operation. This patient was given numerous roentgen treatments recently, with the hope of blocking off the corneal vessels, and a second transplantation was planned. I am happy to see that Dr. Scheie has done this operation and I hope that his results are satisfactory. I

also hope that he will do a similar operation on the other eye, which is less scarred and vascular and offers a better prognosis.

DR. W. E. FRY: A number of cases of interstitial keratitis have occurred at the Overbrook School; and, in breaking down some of the statistical data on them several years ago, I found that the general outlook for corneal surgery was poor. Many of the eyes showed evidence of severe anterior uveitis and, when the fundus was visible, optic nerve atrophy.

The way in which the transplant acts as a foreign body in the cornea is probably not fully understood. A case may be cited. A youngster with interstitial keratitis on both of whose eyes I did a transplantation had postoperative vision of 6/9 in one eye and maintained this vision for over one year. Six months later I operated on the second eye with exactly the same technic, with no complications. The result was a partially opaque cornea and vision of 6/60. I cannot explain the difference in results. There may be something about the selection of donor material which is not understood.

DR. WILLIAM HUNT: It has been my privilege to look at all these transplants and to follow them through; while the procedure is not technically very difficult, any one who is not prepared to carry out thorough and meticulous after-care should not attempt it.

I believe that Dr. Scheie said there were 60 complications in this series. I think we can evaluate this operation as a practical, useful procedure which should be tried in favorable cases.

DR. LOUIS LEHRFELD: My first oldest case of corneal transplantation on record dates back to 1940. In this case, one of keratoconus, the operation was regarded as fairly successful. The patient's vision was partially restored by reason of the transplant. When I saw the patient only a few weeks ago in the clinic, keratoconus was recurring in the transplant itself. I mention this because it should be kept in mind that mere transplantation of a good cornea to take the place of an old one does not necessarily change the pathologic condition underlying the keratoconus. This does not mean that one should be discouraged in performing this operation for keratoconus of any other cause.

Dr. Scheie has suggested various types of corneal lesions for which he would propose doing a corneal transplantation. Of course, it has been said facetiously that when one gets good results with transplantation one wonders whether similar results could not have been obtained with some other treatment. I should like to encourage further experimental work on corneal transplantation, for the future holds much for it. Despite the fact that there are many disappointments, I feel that there will be many more cases in the future, even in group 3 and 4, in which transplantation will be successful.

DR. HAROLD G. SCHEIE: Vascularization of the transplanted cornea is the greatest problem with which one has to deal. The explanation of this vascularization has always been obscure, but it might be derived from the experience of the general plastic surgeon who finds that skin transplanted from one person to another apparently takes well for approximately three weeks. After this, it exfoliates and is lost, not being tolerated by the recipient's tissues. It is at about the same interval that

eyes on which corneal transplantation has been done become red; the graft tends to become cloudy, and blood vessels invade the cornea. This reaction and vascularization are less severe in corneas in which vascularization has been minimal before operation. On the other hand, when the cornea has previously been heavily vascularized, the eye seems to do well for two to three weeks; then it becomes inflamed, and the graft vascularizes rather rapidly. As a result, the transplants become opaque in a rather large number of cases. The reaction of the recipient to tissues from another of the same species might well be correlated with the number of preexisting vessels in the recipient bed, the tissue responses being greater where vascularity is excessive.

Some Observations on Miotics. Dr. Edwin B. Dunphy.

This paper was published in the March 1949 issue of the *American Journal of Ophthalmology*, page 399.

DISCUSSION

Dr. Francis Heed Adler: We are all appreciative of the able way in which Dr. Dunphy has covered both the theory and the practical use of miotics. His warning about methacholine (mecholyl®) is evidence that the increased pressure in glaucoma damages the postganglionic fibers, so that the myoneural junction becomes sensitive to cholines.

Dr. Scheie has previously reported the experimental production of sensitivity to methacholine in cats by artificially raising the intraocular pressure for short periods. It is generally supposed that such sensitization does not occur until nerve fibers have degenerated; if this is so, one would hardly expect methacholine to be of use in acute glaucoma when the attack has lasted only an hour or so. Actually, it does seem to be effective in this condition, and this, combined with Dr. Scheie's experiments, suggests that it is not necessary for nerve degeneration to take place in order that sensitivity be produced.

Dr. Irving H. Leopold: I was interested in Dr. Dunphy's discussion on triethyl pyrophosphate. In 1934 there was an epidemic of diarrhea and peripheral palsies among the inhabitants of one of the islands of the West Indies, and for a long time there was uncertainty as to the etiology. It was then found that the afflicted persons were eating or working with Jamaica ginger; I believe one of the compounds which was extracted from the ginger was triorthocresyl phosphate. Only a few years ago, some Swedish workers found that this drug had a strong anticholinesterase activity. It may be that this drug, or one of its derivatives, also might merit evaluation in ophthalmology.

Dr. Dunphy considered the question of synergism of cholinergic and anticholinesterase drugs. It is interesting to consider the effect of combining two anticholinesterase drugs, such as physostigmine and di-isopropyl fluorophosphate. It can be shown that physostigmine blocks the action of di-isopropyl fluorophosphate. A series of animals were given injections of the latter, and the LD_{50} was determined. If another series of animals were given a sublethal injection of physostigmine, it was found that the previously used dose of di-isopropyl fluorophosphate no longer killed those animals. In other words, phy-

sostigmine had protected the animals from the lethal action of di-isopropyl fluorophosphate. The same phenomenon can be demonstrated in the eye by instilling a drop of physostigmine salicylate in one eye of a subject, waiting until the maximal miotic effect has occurred, which usually takes about fifteen minutes, and then instilling a drop of di-isopropyl fluorophosphate in each eye. The eye which has received physostigmine comes back to the preinstillation size in two or three days. The eye which has received di-isopropyl fluorophosphate alone remains miotic a week or two, the usual length of time for the miotic effect of this drug.

Now, what about the reverse effect, that is the effect of physostigmine when di-isopropyl fluorophosphate precedes it? The sublethal dose of physostigmine is determined—that is, the intramuscular dose that just fails to kill. The animals are given an injection of di-isopropyl fluorophosphate in a similar sublethal dose. After this the previously determined sublethal dose of physostigmine is injected. The injection of physostigmine now results in the death of most of the animals. In other words, di-isopropyl fluorophosphate does not prevent the action of physostigmine. Actually, when physostigmine is given after di-isopropyl fluorophosphate, there is a combined effect.

An experiment that interested me was the ingenious method of instilling eye drops in the dark. The observation that di-isopropyl fluorophosphate constricted the pupil of the dark-adapted eye does not mean that this drug has a direct effect on the musculature of the iris, but simply that even the dark-adapted eye produces acetylcholine that can be conserved when di-isopropyl fluorophosphate ties up the cholinesterase.

DR. I. S. TASSMAN: I have under observation at present at Wills Hospital a patient in whom I noted an increase in the intraocular pressure after the instillation of methacholine and neostigmine; in addition, the lens in the affected eye was pushed so far forward that the anterior chamber was almost entirely obliterated. I also recall another patient in whom we observed an increase in the intraocular pressure after the use of di-isopropyl fluorophosphate.

It is interesting to speculate on the mechanism by which the intraocular pressure is lowered by these drugs. As was pointed out, there are certain differences in the action of these various drugs when they are employed in certain combinations. This is probably true of the adrenergic group, as well as the cholinergic group. Sometime ago Dr. Cogan published an article which had to do with the dual innervation of the ciliary body, and in that paper I believe he referred to the use of these miotics (Accommodation and the Autonomic Nervous System, ARCH. OPHTH. **18:** 739 [Nov.] 1937. Myerson and Thau speculated on the possibility that an overaccumulation of the esterases with oncoming age explains the occurrence of presbyopia.

A fair amount of progress has been made since the work of Loewi, Englehart, Cogan and others, but the mechanism is not yet fully understood.

DR. EDWIN B. DUNPHY: I was very much interested in what Dr. Leopold said on the combination of physostigmine and di-isopropyl fluorophosphate.

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Regular Meeting, Jan. 21, 1948

CASE PRESENTATION

Cases of the following conditions were presented and discussed: (1) epithelioma of the orbit in a patient who had previously had an enucleation for an epibulbar Bowen carcinoma; (2) angiospastic retinopathy; (3) aberrant regeneration of the third nerve following a subarachnoid hemorrhage; (4) lesion of the nictitating membrane thought to be Leptothrix conjunctivitis or tuberculosis; (5) choroiditis and secondary glaucoma; (6) granuloma of the sclera, of undetermined origin.

PRESENTATION OF PAPERS

Glaucoma. Dr. Paul A. Chandler, Boston.

In this paper, the second in a series of lectures on the clinical manifestations and treatment of glaucoma, the shallow chamber type of glaucoma was considered. The tension in this type is characterized by a spikelike tonometric curve with wide fluctuations, believed to be due to varying obstruction to the chamber angle. Until synechias have formed, the response to miotic therapy and to surgical treatment is good, much better than that of deep angle glaucoma. Noteworthy is the deepening effect on the anterior chamber which the filtering operations produce. The operation of choice is iridencleisis. The indications for operation are chiefly age and the stage of the glaucoma. Other things being equal, the younger the patient and the more advanced the glaucoma, the greater the indication for operation.

For glaucoma coexisting with, and probably due to, hypermature cataract, the operation recommended is extraction of the lens and wide basal iridectomy in one stage.

Tetraethyl Pyrophosphate: A New Anticholinesterase Miotic. Dr. W. Morton Grant, Boston.

Tetraethyl pyrophosphate is a new and highly active cholinesterase inhibitor which had previously been used as an insecticide but which during the past two to three months has been under investigation at the Howe Laboratory and the Massachusetts Eye and Ear Infirmary as a new agent in the treatment of glaucoma.

In normal eyes, tetraethyl pyrophosphate appeared to compare favorably with physostigmine and di-isopropyl fluorophosphate in miotic activity and to be innocuous to the cornea.

In the treatment of glaucoma in 15 cases, it was observed that where pilocarpine had some effect in lowering tension tetraethyl pyrophosphate was considerably more effective, although administered in a much smaller amount. When used excessively, tetraethyl pyrophosphate produced unpleasant symptoms like those produced by physostigmine and di-isopropyl fluorophosphate. In 2 cases an increase in tension, instead of a decrease, followed application of the drug. A more quantitative comparison of tetraethyl pyrophosphate with other cholinesterase-inhibiting miotics is being carried on at present.

Aphakia. Dr. Alfred Cowan, Philadelphia.

The essayist briefly reviewed the changes in the optical characteristics of an eye that has had a cataract extraction. The retinal image is one-third larger than before operation, and the aphakic eye has no accommodative ability. The change in the principal and nodal points causes a slight change in the visual axis. With removal of the lens the eye becomes many times more sensitive to violet and to ultraviolet light. In addition, nearly every aphakic eye must be considered a mutilated eye. The person who has had a cataract removed has entirely different sight with correction, and it is surprising that such patients are not more confused, and even disappointed with it.

The shape and location of the correcting lens are important, as they may differ from those of the trial lens. One must be certain that the optical axis of the lens coincides with the visual axis, which is frequently not at the center of the pupil, especially when the pupil has been altered. In cases of binocular aphakia, failure to center the lens properly or a considerable difference in the strength or nature of the correcting lenses produces various effects. Tilting of the correcting lens may cause an undesired cylindric effect.

In order to determine the proper correcting lens, the author suggested arranging the plano trial lenses so that the finished spectacle lens can be more closely duplicated in the trial lens combination.

Fused and one piece bifocals can be obtained, but the segment should be so cut that the base is down to neutralize somewhat the strong prism base up present in the lower portion of the distance lens. Therefore, flat top segments are basically wrong in any bifocal glass with convex distance lens. The practicality of cement bifocals should not be overlooked.

Despite reports to the contrary, the essayist stated the belief that correction of monocular aphakia (one eye normal with good vision) is impractical, not only because of the diplopia due to the aniseikonia and prismatic effect of the difference between the glasses but also because one eye has some degree of dynamic accommodation and the other eye no accommodation. Even if the retinal images are made more nearly equal by such means as contact lens or minifying lens, it is possible to superimpose them perfectly only for one distance at a time. Therefore, the binocular vision is not good and may be a cause of discomfort when so obtained. However, if the patient is comfortable with such limited binocular vision, there is no reason that he should not be given it.

In a case of monocular aphakia and immature cataract in the other eye, the eye chosen for correction will usually be the one with the better visual acuity, although sometimes the patient will prefer the eye with the poorer, but more natural, vision. After the combined type of operation, the type and excessive amount of light may be very annoying. Dark glasses to be used when the occasion warrants may be prescribed but should not be given for constant permanent use.

Book Reviews

Vision: Its Development in Infant, and Child. By Arnold Gesell, M.D., Francis L. Ilg, M.D. and Glenna Bullis. Price, $6.50. Pp. 329, with 72 illustrations. Paul B. Hoeber, Inc. (Medical Book Department of Harper & Brothers), 49 E. 33d St., New York 16, 1949.

Prior to this study of Gesell, Ilg and Bullis, there have been remarkably few observations on the development of the visual functions in the infant and child, and none of the comprehensive scope that are reported in this book. The material is well presented, beautifully illustrated and organized into the main headings termed "The Growing Action System," "Developmental Optics" and "Developmental Appraisal." Each subdivision is arranged chronologically according to the age of the child. In keeping with the authors' intention to consider vision in relation to the development of the child as a whole, much of the material, especially in the first half of the book, deals with nonvisual functions.

The subject should be of interest to pediatricians, ophthalmologists, psychiatrists, parents and teachers. The value put on the book will vary according to what one expects from it. The present reviewer, an ophthalmologist, found it disappointing. In it he found inadequate standards of norms, an unsatisfactory bibliography, an unfamiliar vernacular and a plethora of generalizations with an insufficiency of statistically valid data. Especially unpalatable was the chapter on retinoscopy, entitled "The Young Eye in Action," in which purely optical phenomena are endowed with psychic counterparts.

Admittedly a difficult subject, it is nonetheless important; and the authors could make a valuable contribution, what with their admirable perseverance and kinographic technic for studying child behavior. It is to be hoped that their study of vision will be extended, preferably in conjunction with an ophthalmologist who is familiar with the pathologic aberrations, and preferably with full use of such aids for investigating visual function as the opticokinetic response for measuring visual acuity and the bitemporal electrodes for recording ocular movements. Such a study might be expected to give much needed information on the development of vestibular, reflex-visual and voluntary movements of the eyes, cycloplegic refraction of the eye at different ages, and quantitative data on the development of visual acuity, color discrimination, etc. So far as the authors have failed to provide such information, the book fell far short of expectations.

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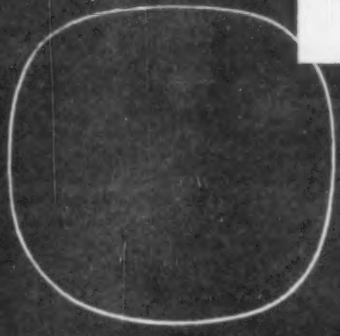

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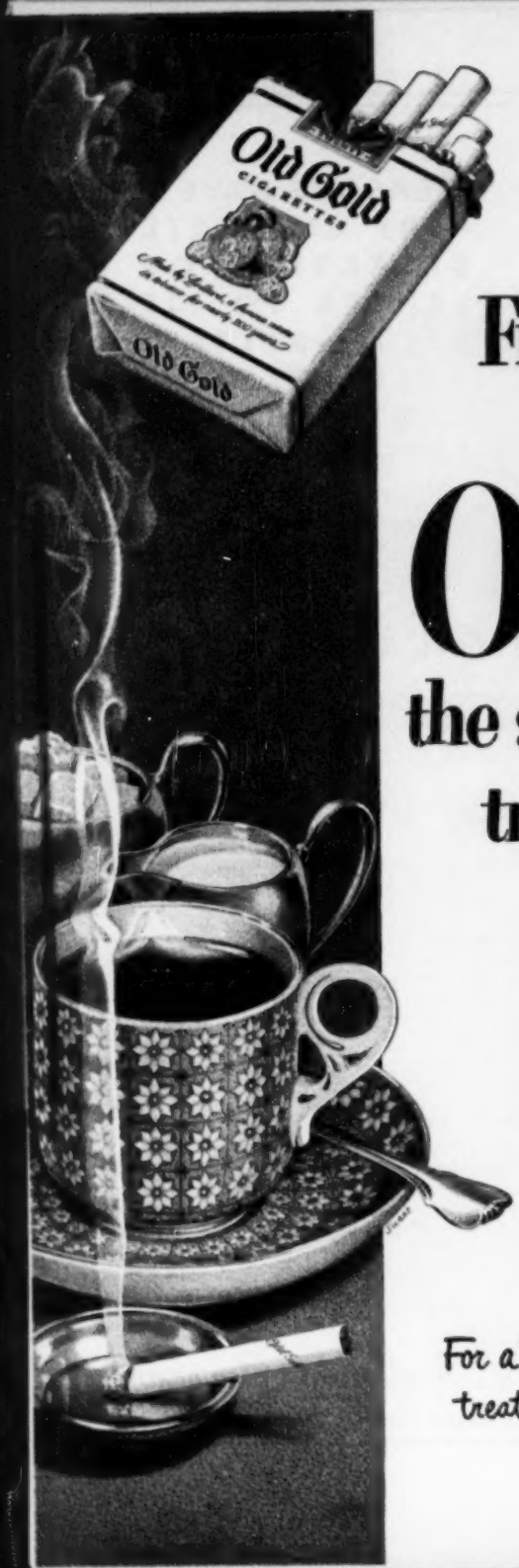

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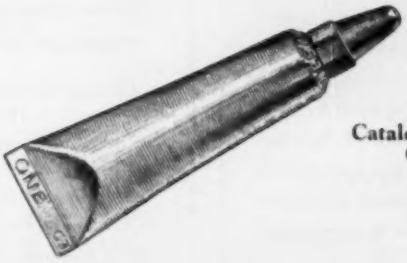

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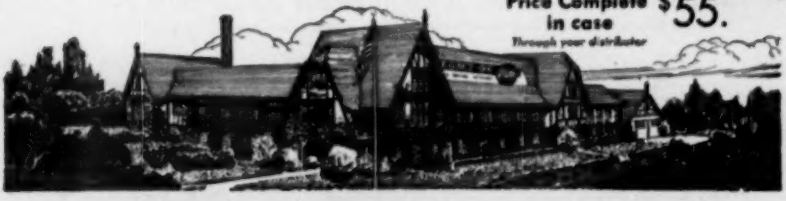

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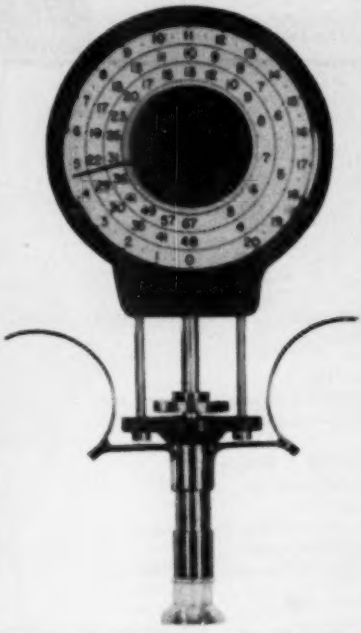

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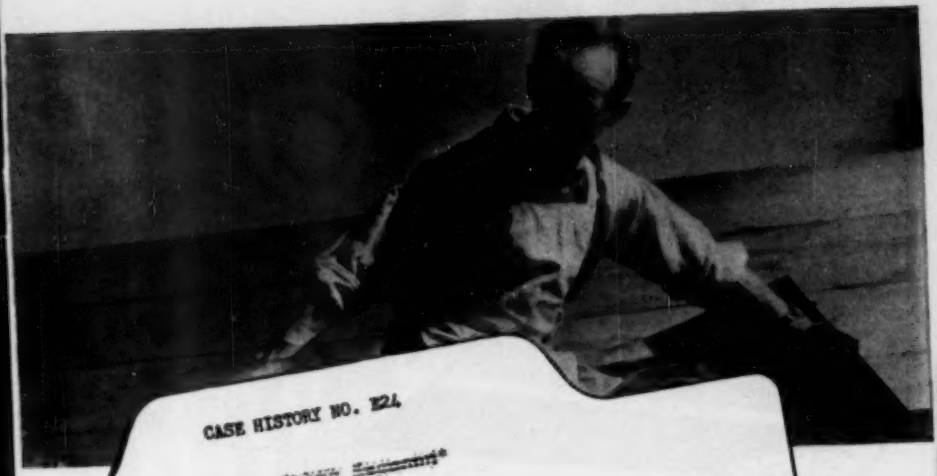

CASE HISTORY NO. E24

Name: [redacted]*
Occupation: Roofer

November 11 — New patient. Complains he never had a pair of glasses that were satisfactory. Has had five pairs in all. Reports involuntary habit of shading eyes with his hand; almost constant squint. Wore following prescription in white crown:

First Rx

O.D. +75 x 75
O.S. +50 x 105

Complete examination revealed patient acceptance of basic prescription. Absorption check test with Soft-Lite Trial Case Accessory indicated definite need for neutral absorption in Soft-Lite shade #2.

November 18 — Fitted patient with following Rx:

Second Rx

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December 12 — Recheck. Patient reports complete relief and states that new glasses are the best he ever had.

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CONTENTS

PAGE

Growth of the Components of the Human Eyeball:

I. Diagrams, Calculations, Computation and Reference Tables. HARRY A. WILMER, M.D., PH.D., PALO ALTO, CALIF., AND RICHARD E. SCAMMON, PH.D., BRAINERD, MO. 599

II. Comparison of the Calculated Volumes of the Eyes of the Newborn and of Adults, and Their Components. RICHARD E. SCAMMON, PH.D., BRAINERD, MO., AND HARRY A. WILMER, M.D., PH.D., PALO ALTO, CALIF. 620

Experimental Study on the Vitreous: II. Experiments on Disappearance of Red Blood Cells from the Vitreous. LUDWIG VON SALLMANN, M.D., NEW YORK 638

General Anesthesia in Cataract Surgery. R. DOUGLAS SARBERS, M.D., AND NORMAN L. CUTLER, M.D., WILMINGTON, DEL. 653

Flicker Fusion Fields: III. Findings in Early Glaucoma. PAUL W. MILES, M.D., ST. LOUIS 661

Use of Curare in Cataract Surgery. DANIEL B. KIRBY, M.D., NEW YORK 678

Retrolental Fibroplasia: A Clinical Study of Two Hundred and Thirty-Eight Cases. MERRILL J. KING, M.D., BOSTON 684

Uses of Naphazoline (Privine®) in Ophthalmology. PAUL HUBWEIT, M.D., CHICAGO, AND JOHN M. THOMPSON, M.D., SOUTH BEND, IND. 707

Photography of the Red Reflex. VIRGINIA LUSKIN, M.D., NEW YORK 718

Glaucoma at the Wills Hospital. LOUIS LEHRFELD, M.D., F.I.C.S., AND OWEN BELMONT, M.D., PHILADELPHIA 720

Scotomas in Conjunction with Streptomycin Therapy: Report of Eleven Cases. EDWIN B. THOMAS, M.D., BOSTON 729

Ocular Lesions Induced by Acute Exposure of the Whole Body of Newborn Mice to Roentgen Radiation. EGON LORENZ, PH.D., AND THELMA B. DUNN, M.D., BETHESDA, MD. 742

Treatment of Occluded Nasolacrimal Ducts in Infants. MARTIN P. KOKE, M.D., SAN DIEGO, CALIF. 750

Corneal Opacity Acting As a Concave Lens: Report of a Case. SAMUEL L. SALTZMAN, M.D., NEW YORK, AND M. ALLEN GREENWOOD, M.D., STATEN ISLAND, N. Y. 755

Frequency of Occurrence of Cataract in Atopic Dermatitis. ALFRED COWAN, M.D., AND JOSEPH V. KLAUDER, M.D., PHILADELPHIA 759

A Contribution to Keratoplasty. K. LINDNER, M.D., VIENNA, AUSTRIA 769

CORRESPONDENCE:

Aureomycin in Treatment of Virus Diseases. GEORGE A. SHERMAN JR., M.D., RED BANK, N. J. 772

NEWS AND NOTES 773

ABSTRACTS FROM CURRENT LITERATURE 775

SOCIETY TRANSACTIONS:

College of Physicians of Philadelphia, Section on Ophthalmology 785

BOOK REVIEWS 792